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COMMON BEHAVIOR DISTURBANCES IN THE FIRST TWO YEARS OF LIFE

BENJAMIN SPOCK, M.D.
Rochester, Minn.

Read Before the Section on Nervous and Mental Diseases at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 13, 1947.

From the Department of Neurology and Psychiatry, the Mayo Clinic, and the Rochester Child Health Project.

Significant behavior disturbances in babies are relatively infrequent during the first year of life as compared with the second, mainly because there are relatively few occasions for conflict between mother and infant. On the other hand, anxiety and weeping spells are common in the mother at the start. In our civilization, she may take her first baby home without any previous experience to accustom and reassure her. Prenatal classes are of some value but do not take the place of that everyday familiarity with the live baby which is the lot of young women in cultures more primitive and communal than ours.

A number of pediatricians, psychiatrists and obstetricians have recently become interested in the possibility of making the lying-in period more natural and reassuring. They have felt that the usual practice of relegating babies to a nursery, from which they are brought to their mothers only at intervals, and the tendency to let breast feeding go by default have inadvertently given the inexperienced mother the initial impression that she is of little importance to her baby and that its care can be entrusted only to medical experts. The so-called "rooming-in" arrangement is being experimented with in Detroit and elsewhere. The baby's crib remains in the mother's room, so that she can become familiar with his noises, moods, movements and appetite, and so that she can feed him on the breast when he is hungry, rather than according to the clock. Preliminary reports suggest that the effect is good, not only on mothers and babies but also on fathers. In conventional obstetric arrangements, the father is apt to feel like a rank outsider, a germ carrier from whom the baby must be shielded. In the "rooming-in" arrangement, he, and he alone, is allowed to visit, which allows him to think of himself as an acceptable member of the family at this formative stage of his development.

There has been a growing tendency in the last few years to discard the rigidity of feeding schedules, which in the past has probably done harm in encouraging mothers to become tense and arbitrary. A number of pediatricians are now recommending that the baby be fed when he seems hungry, irrespective of the hour. Although the method has a solemn name, "the self-demand schedule," and sounds newfangled, it is obviously nature's own, which was used by the entire human race until the turn of the century. A better term might be "self-regulated schedule." Surprisingly, or perhaps not so surprisingly, most babies are found to work themselves onto a fairly regular schedule in a short time. "Rooming in" and "self regulation" appear to be of real value in maintaining the mother's self confidence and giving her a relaxed attitude toward her child.

Feeding problems are the commonest ones during the first year in our culture. A few are started in the first weeks of life if the formula prescribed proves too large and if the nurse or mother has been encouraged to be arbitrary. The baby who, every time he falls asleep satisfied, gets the soles of his feet snapped and the nipple stirred vigorously in his mouth begins to lose his enthusiasm for food and to become balky and irritable. If the resistance to feeding becomes well established, it may last for years and have a harrowing effect on the personalities of child and mother.

A commoner time for feeding rebellion is when solid foods are first introduced. A majority of infants, despite their eagerness for calories, are initially doubtful about the first solid food. The taste, the spoon, the consistency, the method of swallowing are all new. Most of these skeptics decide after a few days that the substance is at least nutritious, and they gradually develop more enthusiasm. An appreciable minority, however, become increasingly intolerant as the days go by. If the struggle is kept up, the mother may report, at the end of ten days, that the baby is beginning to refuse his beloved bottle too. This spreading of the battle is a common phenomenon in children's disorders.

Attempts at forced weaning for which the baby is not ready often cause bad feeling. Psychiatrists have emphasized the danger of too early weaning, especially from the breast. But the exact pathogenesis of a weaning disturbance, as seen by the pediatrician, is not a simple matter of earliness or of deprivation of the breast. In the first place, a majority of young infants who are nursing at both breast and bottle show their ignorance of what is theoretically best for them by preferring the bottle. On the other hand, the baby who has been entirely breast fed for the first three or four months of his life is likely, if the breast supply is plentiful, to object violently to letting a rubber nipple pass his lips, and may prefer to starve for several days.

Some bottle-fed babies show a readiness for gradual weaning to the cup in the period between 8 and 12 months of age. They become less eager for the bottle, stop to play with the nipple and take milk readily from the cup. On the other hand, an appreciable number, even though they have taken willingly a little milk from the cup from as far back as 5 months of age,

will, as they get to be about 9 months old, bat the cup away suspiciously or, pretending they have forgotten what to do, let all the milk run down the sides of the chin. It would seem as though a shrewdness coming on at this stage of development makes them suspect and fear that the bottle is about to be taken away. These are the babies who are generally devoted to the bottle, eyeing it during the solid part of their meal, stroking it and murmuring to it as they drink the contents to the last drop. Forced deprivation of the bottle at such a phase is likely to produce prolonged refusal to take any milk from the cup, unhappy behavior for a number of days and sometimes a complete hunger strike until the frightened mother gives in.

Breast-fed babies, on the other hand, rarely balk at weaning from breast to cup in the last quarter of the first year. In fact, they tend to wean themselves, nursing for shorter periods and gladly taking increasing amounts from the cup. There appear to be at least two reasons why they are more willing to be weaned than are bottle-fed babies of this age. Breast and cup are less similar than bottle and cup. It is the shift to something similar that an opinionated baby resists in weaning. Another factor is the 9 month old baby's desire to be independent during meals. He is now likely to want to sit up for his spoon feeding and, if he is bottle fed, to take the bottle away from his mother's hands and to drink the whole contents while sitting bolt upright. In other words, the breast-fed baby may prefer to wean himself not so much because suckling has lost its charm, but because he has advanced to the stage where he is impatient in the dependent, cuddled position.

The second year brings pronounced changes in an infant's personality and behavior and calls on the mother for entirely new resourcefulness and adaptability. She has become accustomed during the first year to his automatic cooperation. If she offered a teaspoon of spinach, he opened his mouth as eagerly as for applesauce. Even though he liked it less, he was too hungry to quibble. If it was convenient for her to have him in the playpen, she could put him there, toss him a couple of familiar toys and know that he would play happily. But at about a year he acquires independent locomotion and, with it, a charge of energy that keeps him going all day. He explores constantly, shakes table legs, pulls lamp cords, removes every book from the bookcase and climbs on anything he can reach. His ego is taking definite shape. He senses he is a separate person, entitled to wishes and a will of his own. He early learns to say "No" and uses it on all occasions, even in response to suggestions that appeal to him. He has learned no respect for authority and, when told "No, no" from across the room, is more likely to persist than desist. It seems as though he has a compulsive need to exercise his will power for its own sake.

As he becomes more insistent on his independence from his mother, he simultaneously becomes aware of his dependence. He may cry each time she leaves him alone. If he is allowed freedom to explore in the house, he scrambles back to her at regular intervals for reassurance. In the doctor's office he, who at 11 months was quite unconcerned about examination, now leaps to his feet and, yelling, tries to climb off the table into his mother's arms. He is now likely to be frightened by noisy, moving objects, like vacuum cleaners. Undoubtedly, it is part of his total pattern of emotional development that when he has the ability and the desire to explore away from his mother he also has the instinct to hurry back to her noisily when he meets something strange and potentially dangerous.

A majority of babies at about the age of 1 year show the same exaggerated arbitrariness in appetite that they show in other matters. Probably, the smaller rate of gain in weight and the discomfort of molar teething play a part in the sudden decreases in appetite that occur. But, over and above these, he shows an irritating choosiness. He refuses to touch the vegetable which yesterday was his favorite. He may turn against all his vegetables for weeks, and even months, at a time, or against cereal and his milk. The conscientious mother, sure of the importance of the balanced diet, is tempted to become bossy and insistent. The child's temporary dislikes of certain foods are turned into permanent hates, which often last for years. Certainly, more feeding problems begin during the second year than during any other period. The irritation of the frustrated mother and the balkiness of the child easily spread into other aspects of their relationship.

Psychiatrists, from data gained from older children and adults, have stressed the danger to the child's emotional development of too early and too rigorous toilet training. Pediatric observation would indicate that the earliness at which training efforts are begun is much less important than the reaction of the child and the attitude of the mother during the precarious second year. He is generally opinionated and touchy. He becomes increasingly aware of his bowel function and takes a possessive and proprietary attitude toward it. As he slips off the seat, he turns to admire his movement, sniffs it appreciatively and asks his mother to enjoy it too. If her attitude is overdemanding and intolerant, it is easy to see why she rubs him the wrong way. Actually, few revolts occur in the babies whose movements are naturally regular. They have their movements on the seat right after breakfast, before they have a chance to become impatient. It is the child who is naturally irregular whose mother is tempted to put him on too often and to insist that he stay on too long. The babies who are most prone of all to develop resistance are those who have experienced painfully hard movements. In fact, one painful movement may be enough to create a dread of the toilet that lasts six or eight months. Whatever the cause of the initial resistance, the mother's insistence increases the child's obstinacy, anxiety and guiltiness. When he eventually decides to give in and perform in the right place, he may show anxiety about other forms of dirtiness, too. Suppositories and enemas used after a training struggle has begun are resisted with rage and terror and hasten the character distortion.

This vital phase of ego formation is difficult for parents. They are not prepared by experience or teaching for the drastic changes. Arbitrary doctrines about diet and toilet training invite them into trouble. Small houses and apartments provide too few cubic feet per ego and too few harmless outlets for the expanding personality of the 1 year old child. The small number of children per family encourages parental overconcern. There tend to be too many prohibitions, too many demands and too many clashes. The child's outgoingness is blocked; his progress toward independence is impeded, and his awareness of self is intensified beyond what is ideal.

In the olden days, parents with poor qualities of leadership probably relied most on slaps. But the modern teaching that physical punishment is shameful has deflected them into forms of control such as chronic scolding, prolonged moral disapproval, warnings of the dangerous consequences of misbehavior, even excessive reasoning and overexplanation, which I believe bring about worse distortion of the malleable personality. These influences are manifested by the age of 2 years in tense, anxious, dependent, self-centered children and lay the groundwork for the formation of specific neuroses and character disorders.

Although the pediatrician cannot hope to change the mother's basic nature, I believe that he can give her prophylactic advice that minimizes the clashes. He should explain at the start that the baby will be a better judge than mother or pediatrician of how much he needs at each feeding, warn the mother when starting solids to give the child time to get used to them and advise against weaning until the child shows readiness, even though it is not until the middle of the second year. He can explain, before the child reaches the age of 1 year, that appetite is likely to change and that satisfactory substitutes which the child likes can be found. More pediatricians today are advising mothers to omit all toilet training efforts until toward the end of the second year, when the baby's awareness of bowel function and intense desire to imitate may induce him to think up the idea of going to the toilet himself. At least the mother should be warned against beginning her training efforts until she can exactly predict the timing of the movement, either because of the baby's regularity or because he begins to make some sign of readiness. It is possible to help the parent who is unimaginative or insecure to avoid some of the disciplinary clashes by describing how the house must be arranged so that most breakable objects are removed from reach, and enough harmless ones, like pots and pans and magazines, are left near the floor. Then the house-bound child has enough to occupy him without too many prohibitions. When inhibition is started, the main recourse of the parent should be a brisk, friendly removal of the child from the dangerous or breakable object and distraction to something else. Mothers also need to be urged to take small children outdoors often, to let them out of their carriages in places where they can safely be given some freedom and where they can become accustomed to other children.

We need also experimentation with some sort of guidance nursery or guidance playground where 1 and 2 year old children, too young to be left at nursery schools, could come to play.

ABSTRACT OF DISCUSSION

Dr. Karl M. Bowman, San Francisco: This is an ideal paper for every doctor and every parent to read. It shows that material can be presented in simple language and yet be of the highest scientific value; that is something which members of the medical profession, particularly psychiatrists, have not sufficiently learned. It illustrates that a great deal of fine research work can be done when working at a clinical level. Those of us in psychiatry would agree to practically all the things advocated here. This study represents the cooperative type of research in various fields of medicine, and the integration of psychiatry with pediatrics, which many psychiatrists have felt would be valuable for pediatrics and for psychiatry. Pediatrics has suffered from the laying down of rules about feeding, toilet training and the like; if the child did not conform, the fault was his, just as it is in certain types of psychotherapy. At one time, it was the patient's fault if he could not conform to the orthodox psychoanalysis, whereas now, in the recent book by Alexander and French, it is suggested that the treatment should fit the individuality of the patient, unless one is to force a specified type of treatment on the patient. I am particularly in favor of the idea of giving the poor father a little more ego help in this situation, for the common attitude in the hospital is that perhaps the father has had some responsibility for the child but that from now on he is less than nothing. There are two questions that I should like to raise. The first concerns this concept that the child resists being shifted from one thing to another which is similar but accepts more readily something dissimilar. Does Dr. Spock feel that this is a universal rule which would apply to all types of childhood training? If so, it is certainly very important. The statement about scolding and its pernicious effect I endorse heartily, and I should agree both with the chairman and with the author that one can be, incidentally, more brutal to a child with certain types of scolding and tongue lashing than with an ordinary spanking or slapping, and do the child's personality infinitely more harm.

Dr. Frederick H. Allen, Philadelphia: I shall confine my comments to two points brought out in this paper. The first emphasis that Dr. Spock places on the plan of bringing the infant into a more intimate relation with the mother from birth, I think, represents an important departure in this bacteriologic age, in which we have stressed a 100 per cent culture-pure atmospere for a child and some of the important emotional needs of the child and the parent have been neglected. Here, it has been recognized that the infant is a part of the family unit from the very moment of his birth. Here, he emerges as a person, an emergence that can never take place in isolation. His needs from the first moment of living bring him into relation with those who have to satisfy those needs. He gets his first experience in living not in the isolation of the nursery, but in the more intimate connection with the mother, who, at the same time, is getting her first experience with this particular child in fulfilling the important role of being a mother. This procedure recognizes that the mother is really the important person to take charge of the child from the very beginning. The second point is the emphasis that Dr. Spock places on the emergence of the negative in the child toward the end of the first year, and in a somewhat exaggerated way in the second year. Such behavior is the evidence of the emergence of a separate person, who is experiencing the first sense of his power. He exercises it in the very ways that Dr. Spock has so clearly stated. The sensitive understanding of this negative behavior, and the realization of its importance, reflected in the way it is handled, can determine the difference between a child who has a healthy way of asserting himself and one who has to continue and develop unhealthy patterns of saying no. This behavior presents a difficult dilemma for a parent, who must put limits and direction into the life of the child while allowing him some freedom to feel negative. The autocratic parent may try to wipe out this apparent rebellion, and the indulgent or timid parent may fail to provide the support a child needs as he is discovering what he can or cannot do. Both extremes represent a failure to understand the importance of the negative in a child's behavior. It is important that Dr. Spock brought out the relation between dependence and independence and to emphasize that independence really grows out of dependence; dependence is not a phase to rush a child over quickly in the urge to shove him into independent living. The healthy aspect of independence means just what the word itself signifies; independence is always in relation to dependence.

Dr. Benjamin M. Spock, Rochester, Minn.: I am glad that Dr. Bowman caught me in that generalization about babies always resisting more strongly the shift to something similar than to something different. I meant it only in regard to weaning behavior. The bottle-fed baby who refuses milk from a cup will often take it from a spoon. The baby who refuses milk from his regular white cup may take it if it is put into a red cup or if it is changed from warm to ice cold.

LEPTOSPIRAL INFECTIONS

A Survey

JOSEPH G. MOLNER, M.D., M.P.H.
KARL F. MEYER, M.D., Ph.D.
and
HERBERT A. RASKIN, M.S.P.H.
Detroit

From the literature on leptospiral infections in the United States, Weil's disease (spirochetal jaundice) and canicola fever,[1] it would appear that these diseases have been recognized as a problem in preventive as well as curative medicine, as prophesied editorially in THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION ten years ago.[2] The research devoted to this subject since Weil made his clinical observations in 1886[3] has resulted in much valuable information. The spirochete Leptospira icterohaemorrhagiae was established as the causative organism of Weil's disease in 1915.[4] Laboratory methods for its diagnosis were introduced in 1922.[5] The clinical manifestations, pathology, animal reservoirs, epidemiology and geographic distribution have been extensively discussed in the literature.[6] A comparable, but less complete, elaboration of detail is also available for canicola fever.[7]

Despite this wealth of data, however, leptospiral infections still challenge the public health officer, the clinician, the bacteriologist, the laboratorian, the veterinarian—in fact, the entire field of medical science. It is the purpose of this survey to evaluate the all-important role of these infections among the acute febrile diseases and to indicate what steps need be taken to meet this problem.

Although leptospiral infections have been reported from practically every country in the world,[7a] the number of cases in the United States appears to be disproportionately low, especially when compared with the incidence in Continental Europe and Great Britain. In the Netherlands, for example, the diagnosis was established in 808 cases between 1929 and 1937.[7a] In France, 263 proved cases were found in the interval from 1924 to 1932, and there were at least 248 cases in Great Britain between 1924 and 1938.[8] In contrast, examination of the medical literature of the United States revealed only 228 cases reported in this country.[9] Since Ashe and associates[10] have shown that North Americans possess no particular immunity to these infections, and since, as will be shown, there is no evidence of less exposure to leptospiras in the United States, such a discrepancy would seem to be due to failure to recognize or to report cases.

The reason for this failure is twofold. First, the clinical manifestations of these conditions are not well enough known to be considered in the differential diagnosis of acute febrile diseases. Second, and perhaps of greater importance, is the fact that the diagnosis is almost entirely dependent on laboratory findings, and there are few laboratories in the United States adequately equipped to do leptospiral agglutination tests. As a matter of fact, the recent work of Ward and Turner,[11] in Baltimore, and of Tiffany and Martorana,[12] in New York, supports the contention of most authors that leptospiral infections are not difficult to detect if one looks for them. The findings in the Detroit survey, as will be discussed, further support these observations.

It is most likely that only the striking, easily recognized severe forms, with their characteristic jaundice, hemorrhage and renal disorders, have been diagnosed and reported. It is known that mild forms also occur which undoubtedly far outnumber the severe ones. Therefore, since only about one-half the patients with these infections have jaundice, as originally predicated by Weil himself and emphasized by subsequent authors, it is readily understandable that unless physicians are aware of the diseases many cases will pass unrecognized. It is interesting to note that despite the availability of specific laboratory service in the Detroit area, in all 78 cases the diagnosis was made either in the second stage of the disease[13] by agglutination tests or at autopsy.

If earlier diagnosis and more frequent recognition of leptospiral infections are to be accomplished, the icteric and hemorrhagic features must yield to the epidemiologically more important first stage, characterized by sudden onset, severe myalgia, especially in the calves, fever, chills and conjunctival injection. Polymorphonuclear leukocytosis is almost constantly present. Confirmation of diagnosis by laboratory procedures may include blood culture, animal inoculation and serum agglutination tests. The last is considered to be the most dependable means available.

Before discussing the series of 78 cases in the Detroit area, certain characteristics of leptospiral infections reported in the United States may be noted. The first case of leptospirosis in the United States was reported by Stimson in 1905.[14] He observed an organism, which he called "Spirocheta interrogans," in the tissues of a patient who died during an outbreak of yellow fever. Although Stimson failed to recognize the organism, Sellards[15] in 1940 identified it as Lept. icterohaemorrhagiae. Wadsworth and associates[5] in 1922 reported a case of Weil's disease occurring in one of his laboratory assistants, and since that time 228 cases of leptospiral infections have been reported in the medical literature of the United States—222 of Weil's disease and 6 of canicola fever. Tables 1, 2 and 3 present a summary of these cases by geographic location and date of onset.

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1. Other leptospiral organisms of pathogenic importance to man have never been reported in the United States, viz., Leptospira grippotyphosa, Leptospira hebdomidis and Leptospira autumnalis.

2. Spirochetal Jaundice, editorial, J. A. M. A. **109**: 1128 (Oct. 2) 1937.

3. Weil, A. D.: Arch. f. klin. Med. **39**: 209, 1886.

4. Inada, R.; Ido, Y.; Hoki, R., and Kaneko, R.: J. Exper. Med. **23**: 377, 1916. Noguchi, H.: ibid. **30**: 95, 1919.

5. Wadsworth, A.; Langworthy, V.; Stewart, F.; Moore, A., and Coleman, M.: Infectious Jaundice Occurring in New York State: Case of Accidental Infection of Human Subject with Leptospira Icterohaemorrhagiae from Rat, J. A. M. A. **78**: 1120 (April 15), 1922.

6. For the most recent complete résumé of all aspects of these diseases the reader is referred to Bertucci (Am. J. M. Sc. **209**: 86, 1945).

7. (*a*) Walch-Sorgdrager, B.: Bull. Health Organ., League of Nations **8**: 143, 1939. (*b*) Meyer, K.; Eddie, B., and Anderson-Stewart, B.: Proc. Soc. Exper. Biol. & Med. **36**: 17, 1938. (*c*) Tievsky, G., and Schaefer, B.: M. Ann. District of Columbia **13**: 11, 1944. (*d*) Rosenbaum, H. D.: Canicula Fever: Case Report and Review of the Literature, Arch. Int. Med. **78**: 531 (Nov.) 1946.

8. Bruno, F. E.; Wilen, C. J. W., and Snavely, J. R.: Spirochetal Jaundice: Report of Fifteen Cases, Including Two Cases of Leptospira Canicula Infection, J. A. M. A. **123**: 519 (Oct. 30) 1943.

9. Leptospiral infections are not generally viewed by members of the medical profession as "reportable" diseases, even though so designated by law in many states. Thus, data are not available in official compilations of vital statistics. The effect of reporting on "incidence" is illustrated by the experience in the Netherlands.[7a] Whereas in the three year period immediately preceding compulsory notification of these diseases there were reported 69 cases, such reports reached the total of 481 in the following three years.

10. Ashe, W., Pratt-Thomas, H., and Kumpe, C.: Medicine **20**: 143, 941.

11. Ward, T., and Turner, T.: Am. J. Hyg. **35**: 122, 1942.

12. Tiffany, E., and Martorana, N.: Am. J. Hyg. **36**: 195, 1942.

13. This stage is characterized by jaundice, hemorrhage and evidence of renal damage. In the absence of the second stage, the patient enters on convalescence.

14. Stimson, A.: Pub. Health Rep. **22**: 541, 1907.

15. Sellards, A.: Tr. Roy. Soc. Trop. Med. & Hyg. **33**: 545, 1940.

A review of these tables reveals many interesting facts. It is apparent that the period from 1935 to 1941

TABLE 1.—*Cases of Leptospiral Infections Reported in the Literature of the United States According to Date of Onset**

	No. of Cases		No. of Cases
1905	1	1934	5
1922	2	1935	10
1923	0	1936	5
1924	2	1937	14
1925	1	1938	23
1926	3	1939	40
1927	1	1940	33
1928	1	1941	12
1929	2	1942	6
1930	0	1943	1
1931	1	1944	17
1932	2	1945	7
1933	0		

* A total of 189 cases in which date of onset was procurable.

TABLE 2.—*Cases of Leptospiral Infections Reported in the Literature of the United States According to Geographic Location*

	No. of Cases
Louisiana *	33
New York †	33
Virginia ‡	18
California §	17
Maryland ‖	17
Alabama ¶	14
Pennsylvania #	12
Ohio **	12
Georgia ††	10
Colorado ‡‡	7
Rhode Island §§	7
Massachusetts ‖‖	7
District of Columbia ¶¶	7
New Jersey ##	6
Texas ***	4
Wisconsin †††	3
Florida ‡‡‡	3
North Carolina §§§	2
West Virginia ‖‖‖	2
Missouri ¶¶¶	2
Connecticut ###	2
Michigan ‡‡‡‡	1
Nevada §§§§	1
Oklahoma ****	1
Location unspecified ††††	8
Total	228

* (a) Stimson.[14] (b) Durand, J.: New Orleans M. & S. J. **93**: 34 1940. (c) Senekgie, H.: J. A. M. A. **126**: 5, 1944. (d) Dobbs, O., and Jarrell, M.: New Orleans M. & S. J. **98**: 458, 1946.

† (a) Packchanian.[2b] (b) Wadesworth; Langworthy, Stewart, Moore and Coleman.[2] (c) McDowell, E.: New York State J. Med. **25**: 19 1925. (d) Cushing, E. J. A. M. A. **39**: 1041, 1927. (e) Glotzer, S.: J. A. M. A. **110**: 2143, 1938. (f) Farrell, E.: New York State J. Med. **39**: 1909, 1939. (g) Elton, N.: Am. J. Clin. Path. **9**: 219, 1939. (h) Tiffany and Marlorana.[12] (i) Stiles, W., and Goldstein, J.: J. A. M. A. **131**: 1271, 1946.

‡ (a) Packhanian.[1a] (b) Larson, C.: Pub. Health Rep. **56**: 1650, 1941. (c) Bloom, N., and Walker, H.: Virginia M. Monthly **68**: 192, 1941. (d) Reid, J., and Holt, R.: ibid. **68**: 571, 1941. (e) Mulholland, H., and Bray, W.: J. A. M. A. **90**: 1113, 1928. (f) ibid Internat. Clin. **4**: 122, 1937.

§ (a) Larson,[1b] (b) Kilgore, E.: Tr. A. Am. Physicians **52**: 116, 1937. (c) Meyer, Stewart-Anderson and Eddie.[22] (d) Ball, H.: Am. J. Clin. Path. **3**: 283, 1933.

‖ (a) Packchanian[1a] (b) Larson.[1b] (c) Goldberg, H., and Dovens, E.: Bull. Johns Hopkins Hosp. **68**: 112, 1941. (d) Ward and Turner.[11] (e) Bathbun, H., and Wagheistein, J.: Ann. Int. Med. **15**: 295, 1941.

¶ Lester, B.; Denison, B., and Tate, G.: South. M. J. **35**: 325, 1942.

(a) Packhanian.[1a] (b) Larson.[1b] (c) Davis, P., and Davis, M.: Ann. Int. Med. **16**: 569, 1942. (d) Kramer, D.: Pennsylvania M. J. **45**: 1298, 1942. (e) White, J., and Prevost, J.: Ann. Int. Med. **15**: 207, 1941 (f) Havens, W.; Bucher, C., and Reimann, H.: J. A. M. A. **116**: 289, 1941. (g) Hayman, J., and Lynch, F.: Am. J. M. Sc. **173**: 80, 1927. (h) Sailer, J.: ibid. **170**: 332, 1925.

** (a) Larson.[1b] (b) Deubel, H.: Ohio State M. J. **37**: 837, 1941. (c) Jentgen, L.: ibid. **37**: 443, 1941. (d) Ashe, Pratt-Thomas and Kumpe.[10]

†† (a) Larson.[1b] (b) Sheldon, W.: Arch. Int. Med. **75**: 119, 1945.

‡‡ Gaines, A., and Johnson, R.: Arch. Int. Med. **60**: 817, 1937.

§§ Laskey, H.: Rhode Island M. J. **22**: 135, 1939.

‖‖ (a) Packhanian.[1a] (b) Larson,[1a] (c) Jeghers, H.; Houghton, J., and Foley, J.: Arch. Path. **20**: 447, 1935.

¶¶ (a) Packhanian.[1a] (b) Manchester, Larson and Thomas.[23d] (c) Towler, H., and Walker, J.: J. A. M. A. **89**: 86, 1927. (d) Tievsky and Schaefer.[7c]

(a) Packhanian.[1a] (b) Larson.[1b] (c) White and Prevost.[1e] (d) Sailer.[1h]

*** (a) Rosenbaum.[7d] (b) Little, O.: Texas State J. Med. **32**: 305, 1936.

††† Larson.[1b]

‡‡‡ Currens, J., and Woodward, R.: South. M. J. **38**: 811, 1945.

§§§ (a) Leptospirochetosis Ictero-hemorrhagica (Weil's Disease), case reports, North Carolina M. J. **7**: 75, 1946. (b) Thomas, W., and Stringfield, P.: ibid. **7**: 254, 1946.

‖‖‖ Packhanian.[1a]

¶¶¶ (a) Larson.[1b] (b) Blake, F.: New England J. Med. **223**: 561, 1940.

Packhanian.[1a]

**** Bates, C., and Hartnett, W.: J. Oklahoma M. A. **39**: 105, 1946.

†††† (a) Editorial, J. Am. Vet. M. A. **108**: 166, 1946. (b) Lorenz, G.: U. S. Navy M. Bull. **42**: 560, 1944.

TABLE 3.—*Cases of Leptospiral Infections Reported in the Literature of the United States According to Month of Onset**

	No. of Cases		No. of Cases
January	6	July	17
February	7	August	21
March	5	September	24
April	2	October	8
May	7	November	9
June	15	December	6

* A total of 127 cases in which month of onset was procured.

represents one of increased case finding, reflecting a general interest in these infections at that time, both in this country and abroad.[16] Cases have been reported from twenty-three states and the District of Columbia, but over 70 per cent of the cases occurred in only nine states. The seasonal distribution of these cases (table 3) compares favorably with reports from other countries, 60.6 per cent occurring in the four month period between June and September. Of the 228 reported cases, in only 178 was the end result of the illness discussed. In this series the fatality rate was 24.7 per cent.

Although the 78 cases of leptospiral infection in the Detroit area[17] represent over one-fourth the total number of cases reported in the United States, this need not imply an increased incidence in this area. It is probably indicative of a high degree of interest motivated by the availability of complete, adequate and specific laboratory facilities in Detroit.[18] Thus, the diagnosis was established in many clinically and epidemiologically suspected cases which undoubtedly would otherwise have been missed.

Despite the apparent awareness of these diseases and the immediate availability of laboratory aid, jaundice developed in all 78 cases. As a matter of fact, it has been repeatedly stated that jaundice was the lead that brought these diseases to differential diagnosis and the accessibility of laboratory agglutination tests, dark field examination, cultures and animal inoculation established the diagnosis. In view of the opinion previously stated that in only about one-half the cases of these infections is jaundice present as a clinical entity, it is obvious that even the relatively large incidence reported from this area is still a significant understatement of the facts.

It should be noted (table 4) that this series of 78 cases includes only proved cases of leptospirosis, verified by an agglutination titer of diagnostic significance (1:300+) or by autopsy. Many cases in which the diagnosis was based on clinical observation without laboratory confirmation are not included. Thus, it may be assumed that had laboratory examination been made in these instances the number of cases reported would have been appreciably increased.

EPIDEMIOLOGY

Age and Sex Incidence.—Because of an occupational predisposition, these infections would seem to be most

16. It was usual to find that the first case reported in a given area was followed by publication of additional cases.

17. Of the cases reported in the Detroit area, 13 have been previously published. Molner and Kasper,[20a] Molner and Meyer,[20c] Martmer,[20b] Clapper, M., and Myers, G. B., Clinical Manifestations of Weil's Disease with Particular Reference to Meningitis, Arch. Int. Med. **72**: 18 (July) 1943. Gordon, W. H., and Feldman, N.: M. Rec. **51**: 209, 1940.

18. The Detroit Department of Health has had such facilities available since 1937 in its own laboratory and in cooperation with the National Institute of Health, Washington, D. C., and the George William Hooper Foundation, University of California.

TABLE 4.—*Cases of Leptospiral Infections in the Detroit Area*

Case No.	Sex	Age	Onset of Illness	Outcome of Illness	Agglutination Reaction: Lept. icterohaemorrhagiae	Agglutination Reaction: Lept. Canicola	Exposure to Leptospiras
1	M	46	July 1937	Recovery	1:30,000	—	Poultry worker
2	M	16	June 1938	Recovery	1:3,000	1:300	Cadet; waded in Rouge river; pet dog had positive agglutination reaction to Lept. icterohaemorrhagiae (1:100,000)
3	M	34	November 1938	Fatal	1:10,000	—	Poultry worker
4	M	17	August 1938	Recovery	1:30,000	—	Moved wet lumber contaminated with rat urine; waded in Clinton river
5	M	38	October 1938	Recovery	1:10,000	—	Dug cesspool in trailer camp, wading in Fox creek, a sewer outlet
6	M	3	January 1938	Fatal	1:30,000	—	Pet dog ill with Weil's disease; neighborhood rats positive agglutination reaction to Lept. icterohaemorrhagiae
7	F	14	March 1938	Recovery	1:20,000	—	Unknown
8	M	32	February 1938	Recovery	1:30,000	—	Poultry worker
9	M	29	November 1939	Recovery	1:30,000	1:100	Poultry worker
10	M	46	September 1939	Fatal	1:30,000	—	Poultry worker
11	M	27	June 1939	Fatal	1:30,000	—	Poultry worker
12	M	49	November 1939	Fatal	1:300	—	Set and handled traps in rat-infested beer garden
13	M	55	December 1940	Recovery	1:100,000	1:100	Poultry worker; home also infested
14	M	21	January 1940	Recovery	1:30,000	1:10,000	Poultry worker
15	M	50	October 1940	Fatal	1:1,000	1:300	Plumber; frequent basement jobs; also trapped rats at home
16	M	47	June 1940	Recovery	1:30,000	—	Trapped rats at home; heavy infestation of food, etc.
17	M	41	May 1941	Recovery	1:30,000	1:300	Home infestation; rat bite 6 wk. previously
18	M	46	January 1941	Recovery	1:10,000	1:300	Poultry worker
19	M	64	February 1941	Fatal	1:30,000	—	Unknown
20	M	39	November 1941	Recovery	1:100,000	1:1,000	Washed automobiles in rat-infested garage
21	M	37	November 1941	Recovery	1:100,000	1:100	Junk collector; killed rats in alley; constant contact
22	M	51	June 1941	Recovery	1:1,000	1:30	Porter in rat-infested apartment; resides in "flophouse"
23	M	52	November 1941	Recovery	1:100,000	1:1,000	Slaughterhouse worker; rats also found in bedroom
24	M	39	August 1941	Recovery	1:100,000	1:100	Washed automobiles in rat-infested garage; home infested; in food, etc.
25	M	57	August 1941	Recovery	1:10,000	1:300	Fish market worker; sets and cleans traps
26	M	7	July 1941	Recovery	1:100,000	1:100	Swimming in Rouge river
27	M	33	December 1941	Recovery	1:100,000	1:1,000	Worked in rat-infested packing room in bottling works
28	M	40	December 1941	Recovery	1:100,000	1:1,000	Poultry worker
29	M	38	May 1941	Recovery	1:800	1:200	Poultry worker; pet dog killed rats, ill
30	M	47	June 1942	Fatal	1:30,000	—	Ground wire man, frequently worked in alleys
31	M	46	January 1942	Fatal	1:30,000	1:30	Alley picker; storeroom infested with rats
32	M	50	December 1942	Fatal	1:30,000	—	Resided in "flophouse"
33	M	38	September 1942	Recovery	1:30,000	—	Poultry worker
34	M	33	August 1942	Recovery	1:30,000	1:100	Fish market worker
35	M	31	September 1942	Fatal	1:30,000	—	Poultry worker
36	M	18	May 1942	Recovery	1:30,000	1:100	Frequently played in alley
37	M	46	August 1942	Recovery	1:30,000	1:10,000	Porter in rat-infested beer garden
38	M	28	July 1942	Recovery	1:100,000	1:2,000	Alley picker; resided in "flophouse"
39	M	51	March 1942	Recovery	1:30,000	1:3,000	Poultry worker
40	M	39	August 1942	Recovery	1:30,000	1:100	Fish market worker
41	M	23	March 1942	Recovery	1:30,000	—	Home and neighborhood infested with rats
42	M	30	October 1942	Fatal	—	1:10,000	Dog kennel in yard; numerous rats
43	M	39	October 1942	Fatal	1:300	1:100	Unknown
44	M	44	October 1943	Recovery	1:30,000	—	Poultry worker
45	F	35	March 1943	Recovery	1:1,000	—	Neighborhood and home infested
46	M	45	August 1943	Fatal	1:1,000	1:10	Unknown
47	M	49	January 1943	Fatal	1:30,000	—	Pet dog positive agglutination reaction to Lept. icterohaemorrhagiae
48	M	28	July 1943	Fatal	1:3,000	1:30	Neighborhood and home infested
49	M	26	August 1943	Fatal	1:10,000	—	Unknown
50	M	9	November 1943	Recovery	1:30,000	—	Neighborhood and home infested; scratched by sick cat
51	M	55	July 1943	Fatal	Autopsy	..	Factory tunnel protection, job site and home infested; three cats ill; pet dog killed rats
52	M	31	August 1944	Fatal	Autopsy	..	Resided in "flophouse"
53	M	57	September 1944	Recovery	1:30,000	1:30	Launderer in slaughterhouse; dirty clothes left overnight
54	M	59	July 1944	Fatal	1:1,000	1:30	Plumber; frequent jobs in basements
55	M	54	March 1944	Fatal	1:30,000	—	Resided in old rat-infested barn in city food prepared here
56	M	41	August 1944	Fatal	1:1,000	—	Home infested; "scratched while in bed"
57	M	47	October 1944	Recovery	1:30,000	1:300	Junk dealer; alley collection
58	M	46	May 1944	Fatal	Autopsy	..	Cook in rat-infested building
59	M	37	November 1944	Fatal	1:30,000	—	Dog ill from rat bite
60	M	39	September 1944	Recovery	1:30,000	1:1,000	Tanner; dead rats found in vats
61	M	18	November 1944	Recovery	1:30,000	—	Cleaning drugstore basement; porter
62	F	26	September 1944	Fatal	1:300	1:30	Home infestation
63	M	50	May 1944	Fatal	1:300	—	Unknown
64	F	49	October 1944	Fatal	1:10,000	1:30,000	Poultry worker
65	M	40	June 1944	Fatal	Autopsy	..	Unknown
66	M	44	March 1944	Fatal	Autopsy	..	Home and job site at foundry infested
67	M	34	November 1945	Recovery	—	1:1,000	Cement finisher, basement work; home infested
68	M	42	October 1945	Recovery	1:1,000	1:1,000	Poultry worker
69	F	39	September 1945	Recovery	1:300	1:10,000	Dishwasher
70	M	54	March 1945	Fatal	1:10,000	—	Contractor, building basements, sidewalks, etc.
71	M	56	August 1945	Recovery	1:3,000	1:1,000	Poultry worker
72	M	43	March 1945	Recovery	1:3,000	1:30,000	Slaughterhouse worker
73	M	41	February 1945	Fatal	1:800	1:1,000	Pet dog ill 2 wk. prior to patient's onset
74	M	21	September 1945	Recovery	1:1,000	1:10,000	Slaughterhouse worker
75	M	53	January 1946	Recovery	1:10,000	—	Plumber, frequent jobs in basements
76	M	49	January 1946	Recovery	1:10,000	1:300	Walked in rat-infested alley in bare feet
77	M	45	October 1946	Recovery	1:1,000	—	Fish cleaner and peddler
78	M	24	April 1946	Recovery	1:1,000	—	Slaughterhouse worker

prevalent among men; and, indeed, such was the case in this series (table 5). Among the 78 cases reported, 73 of the patients were male (93.4 per cent) and only 5 female. The age distribution of these cases provides further evidence of an occupational relationship. It may be noted that 89.7 per cent of the cases occurred in the employable age groups over 20 years of age. A similar age-sex distribution was found to exist among the reported cases in the United States.

TABLE 5.—*Cases of Leptospiral Infections in the Detroit Area: Distribution by Age Groups*

Age Group	No. of Cases	Per Cent, Total
All ages	78*	100.0
Under 10	3	3.8
10 to 19	5	6.4
20 to 29	10	12.8
30 to 39	20	25.6
40 to 49	24	30.8
50 to 59	15	19.2
60 plus	1	1.3

* The series includes 5 female patients, aged 14, 26, 35, 39 and 49.

Seasonal Aspects.—Leptospiral infections generally show no definite seasonal variation, although many authors report a higher incidence between June and November, the largest number occurring in July, August and September. Such reports have usually been based on the work of Walch-Sorgdrager,[7a] of the Netherlands. In the United States, as previously indicated, cumulative reports show a larger proportion of cases in the months of June through September. However, in the Detroit series this was not so. Table 6 shows the appearance of sporadic cases throughout the year, except for an almost imperceptible increase during the period from August through November.

TABLE 6.—*Leptospiral Infections in the Detroit Area: Distribution by Month of Onset*

Month	No. of Cases	Per Cent, Total
Total	78	100.0
January	7	9.0
February	3	3.8
March	8	10.3
April	1	1.3
May	5	6.4
June	7	9.0
July	5	6.4
August	11	14.1
September	8	10.3
October	9	11.5
November	10	12.8
December	4	5.1

Fatality Rate.—As was previously stated, the fatality rate for cases reported in the United States literature is approximately 25 per cent, whereas among the 78 cases in the Detroit area there were 31 deaths, a rate of 39.7 per cent. Variations in virulence and susceptibility[19] may explain the difference between the two rates. However, it has been indicated that the Detroit series represents only severe forms of leptospiral infections, forming a group in which a high fatality rate would be expected.

All authors agree that most of the known infections with Lept. icterohaemorrhagiae come from direct contact with the excreta of rats; recent evidence indicates that dogs are susceptible to this infection from contact with rats and may act as an intermediary between the rat and man.[20] These animals carry the organisms the epithelium of the renal tubules and excrete them with the urine. Soil, food and water so contaminated can become potent sources of infection.

Rats from all parts of the world have been examined, and as high as 48 per cent of the rats examined have been found to be vectors of Lept. icterohaemorrhagiae.[21]

Lept. canicola produces a disorder in dogs that resembles human icteroid infections; and Schuffner,[24] In 1938, Meyer and associates[22] reported renal leptospiral infections in 16 per cent of rats from the Detroit area and a sample survey conducted by the Detroit Department of Health in 1939 showed that about 25 per cent of the rats in this area were carriers of the organism. Positive serum agglutination reactions in dogs have been reported from many areas of the United States, with rates as high as 38.1 per cent.[23] Walch-Sorgdrager[7a] and Meyer and associates[7b] were able to isolate Lept. canicola from persons with an infection resembling Weil's disease. Presumably, Lept. canicola is a canine infection transmissible to man through close contact with the dog.

Most cases of leptospiral infections reported from all over the world show a close association with rats, dogs or their infected excreta, usually in moist, damp or wet environments. In other cases the disease has been contracted while swimming or bathing or from accidental immersion in polluted bodies of water. Certain occupations show an increased degree of exposure to these organisms, and Stiles and associates[20e] discussed these diseases as a compensable occupational hazard. The cases reported from the Detroit area show the same epidemiologic features.

TABLE 7.—*Leptospiral Infections in the Detroit Area: Summary by Manner of Exposure to Leptospiras*

Occupational exposure		49
Poultry worker	18	
Slaughterhouse worker	5	
Alley worker *	5	
Fish house worker	4	
Porter	4	
Plumber	3	
Cement worker	2	
Auto washer	2	
Packing room	1	
Factory tunnel protection	1	
Tanner	1	
Cook	1	
Dishwasher	1	
Foundry	1	
Neighborhood and residence infestation		12
Accidental immersion in water		4
Pet dog		4
Accidental contact in alley		2
Unknown		7

* These include rag picker, alley picker, junk peddler and ground wireman.

19. Strong, R., in Stitt's Diagnosis, Prevention and Treatment of Tropical Diseases, ed. 6, Philadelphia, The Blakiston Company, 1942, vol. 1, p. 389.

20. (*a*) Molner, J. G., and Kasper, J. A.: Outbreak of Jaundice in Detroit: Preliminary Report, J. A. M. A. **110**: 2069 (June 18) 1938. (*b*) Martmer, E.: J. Pediat. **14**: 48, 1939. (*c*) Stiles, W. W., and Sawyer, W. A.: Leptospiral Infection (Weil's Disease) as an Occupational Hazard, J. A. M. A. **118**: 34 (Jan. 3) 1942. (*d*) Alston, J., and Brown, H.: Proc. Roy. Soc. Med. **30**: 741, 1928; Lancet **1**: 569, 1937. (*e*) Raven, C.: J. Infect. Dis. **69**: 131, 1941.

21. Walch-Sorgdrager,[7a] Meyer and others.[7b] Ido, Y.; Hoki, R.; Ito, H., and Wanti, N.: J. Exper. Med. **26**: 341, 1917. Larson, C.: Pub. Health Rep. **58**: 949, 1943.

22. Meyer, K.; Stewart-Anderson, B., and Eddie, B.: Am. J. Pub. Health **29**: 347, 1939. (*b*) Packanian, A.: Pub. Health Rep. **56**: 2145, 1941. (*c*) Meyer and others.[22] (*d*) Manchester, B.; Larson, C., and Thomas, L.: M. Ann. District of Columbia **13**: 133, 1944. (*e*) Molner[20a] and Meyer, K.: Am. J. Pub. Health **30**: 509, 1940. (*f*) Raven.[20e]

24. Schuffner, W.: Roy. Soc. Trop. Med. & Hyg. **38**: 7, 1934.

Table 7 is a summary of the cases reported in this area grouped according to the manner of exposure to the leptospira, as determined by epidemiologic investigation of each case by the staff of the Detroit Department of Health. With the exception of the 7 cases of unknown exposure (table 4), in every instance there was found the characteristic contact with rats and/or dogs. The emphasis placed on occupational exposure is evident here in the fact that 49 persons (62.7 per cent) had been so exposed. Each of these patients gave a history of rat infestation of his job site. In addition, 9 persons also gave a history of rat infestation of their place of residence and residential neighborhood, thus presenting a dual possibility of exposure to the organism. The predominance of poultry workers among the first patients whose disease was diagnosed in this area led to an interesting experiment conducted by us in which leptospiras were discovered on the work tables of these establishments.[25]

In all the cases in which rat-infested homes were reported, contamination of food, presence of rats in bedrooms and bathrooms, handling of rat traps and carcasses and other sources of exposure were indicated (table 4). In 3 of the cases in which pet dogs were handled, the dogs showed positive agglutination reactions, while in a fourth the dog became ill after a rat bite. In the last case, rats trapped in the neighborhood gave positive agglutination reactions, and the organism was demonstrated in macerated specimens of the kidneys. Contact with pet dogs was also a possible source of exposure in 4 additional cases.

In the cases in which exposure apparently resulted from accidental immersion in polluted water, rats trapped in the immediate area were studied and leptospiras were demonstrated in each case. Of the 7 cases with unknown history, 6 were fatal, with death intervening before any epidemiologically valid history could be obtained. In the remaining case (7, table 4) no definite exposure to either rats or dogs was revealed.

Thus far, the epidemiologic factors of age, sex, seasonal variation and manner of exposure to leptospiras have been discussed. It has been indicated that, with only minor variations, the cases in the Detroit area were similar to those reported elsewhere in the United States and other parts of the world. But with further correlative analysis of the agglutination reactions and the manner of exposure to leptospiras (table 4), certain questions arise relative to the differential diagnosis of infections with Lept. icterohaemorrhagiae and Lept. canicola and the epidemiologic relationships of these organisms.

Clarification of the relationship of Lept. icterohaemorrhagiae and Lept. canicola has yet to be determined. Various conflicting factors must be reconciled. Some authors claim a strong cross agglutination factor between the two organisms,[7a,e] while others (Rosenbaum [7d]) consider that only a mild coreaction exists.[26] Further, the effects of various strains of the organisms, their antigenic qualities and the potential production of antibodies require further study. In addition, the time of withdrawal of serum during the course of illness also greatly complicates the differential diagnosis.

At first it was believed that Lept. canicola was merely a variant of Lept. icterohaemorrhagiae. Morphologically, even with the electron microscope,[27] the two organisms appear identical. At present, however, it is generally agreed that leptospirosis canicola represents a distinct disease in that it varies from typical Weil's disease immunologically, in mortality rate, in its virulence in test animals and in some clinical characteristics.[7a,d]

In 38 cases of the Detroit series, it is obvious that the infection is that of Lept. icterohaemorrhagiae Agglutination reactions for Lept. canicola in these cases were either negative or the titers extremely low (less than 1:30) [28] In 2 additional cases (42 and 67, table 4) the diagnosis was clearly one of leptospirosis canicola. In the 5 cases in which the diagnosis was made at autopsy, identification of the specific organism was, of course, impossible.

However, the exact differential diagnosis in the remaining 33 cases is not so clear. As indicated in table 4, the agglutination titers of the serums of these patients are of apparently diagnostic significance against strains of both Lept. icterohaemorrhagiae and Lept. canicola. Which of these cases represent infection predominantly with Lept. icterohaemorrhagiae or Lept. canicola, and which cases represent mixed or dual infections is difficult to say.

According to the work of Walch-Sorgdrager,[7a] confirmed by Meyer and associates, there are cases in which one serum reacts with another strain in a manner which is termed para-specific (associated reaction), since it rests on the similarity of the two strains in respect to their antigenic structure. It has been shown that both rat and human strains of Lept. icterohaemorrhagiae give paraspecific reactions with Lept. canicola serum. At times, this reaction has been very strong, yielding a value up to one-third the specific titer. The titer generally served to distinguish between these paraspecific reactions and the main (specific) reaction. Identification of the organism was possible from the fact that the reaction reached the level of the full specific titer with one or more anti-leptospira-icterohaemorrhagiae serums, but did not with the anti-leptospira-canicola serum, and also from the fact that the paraspecific reaction was apt to be weaker when the test was repeated or when a serum produced with heated antigen was used. Except for this difference in titer, the main and the paraspecific reactions cannot be distinguished with certainty.

25. In the poultry houses studied there was found a heavy rat infestation, due to general lack of good housekeeping, blood, water and offal not being completely removed. The work tables were washed with Ringer's solution early in the morning, after having been exposed, as was the usual practice, during the night. Inoculations were made in guinea pigs, resulting in jaundice and death, with the pathologic lesions of Weil's disease. At a later date, after the normal day's labor had been completed, one table top was washed with a dilute solution of hydrochloric acid. The following morning no leptospiras were demonstrable in sample washings. This seems to verify other experimental and epidemiologic observations that leptospiras do not remain viable in an acid medium.

26. In certain of the agglutination reactions indicated in table 4, the titers could perhaps be explained on a cross agglutination basis. But there are others that show a very high dilution for Lept. icterohaemorrhagiae and a negative reaction for Lept. canicola. This merely complicates the picture a little more.

27. Morton, H.: J. Bact. 45: 143, 1943.

28. Blood serums from the 78 cases underwent agglutination tests for both Lept. icterohaemorrhagiae and Lept. canicola. These tests were conducted in the laboratory of the Detroit Health Department; at the National Institute of Health, in Washington, D. C., or at the George William Hooper Foundation, at the University of California; in many instances a single serum was examined at all three laboratories. Unfortunately, the agglutination reaction for Lept. icterohaemorrhagiae in most instances does not represent the "end point" of the reaction but merely an arbitrary "stopping point." Thus, it is impossible to derive a true representation of the relationship of the immunologic characteristics of these organisms from these data.

It would, therefore, seem probable that in many of these 33 cases the infection was with Lept. icterohaemorrhagiae and that the agglutination reaction noted represented merely a paraspecific reaction with Lept. canicola. There is always a possibility that the paraspecific reactions are anamnestic, since Lept. canicola infections may be latent. Man is probably frequently exposed to, and even infected with, these organisms Repeated serologic tests in combination with absorption undoubtedly would have confirmed the etiologic agent in these infections. Unfortunately, records for repeated agglutinations in the Detroit series are not available.

Unless one of these presumptive explanations is admitted for all these cases, the epidemiologic characteristics of Lept. canicola infections must be subjected to reconsideration. Although Lept. icterohaemorrhagiae is known to infect many animals (dogs, field mice, cats, pigs, foxes, mongooses, poultry, bandicoots, horses and rats), Lept. canicola has never been shown to infect naturally any animal but the dog. Lept. canicola has never been demonstrated in the rat population.[29] Even experimental inoculation of rats by Walch-Sorgdrager showed that whereas the rat was nearly always a carrier of Lept. icterohaemorrhagiae, it did not become a carrier of Lept. canicola. The latter organism appeared in the kidney of this animal only transiently and was not excreted in the urine.

It is interesting to note that even though 35 patients showed positive agglutination reactions with Lept. canicola in dilutions of 1:100 or more, only 4 of these patients indicated possible exposure to leptospiras from dogs, the remainder indicating known exposure to rats exclusively. Although contrary to all existent laboratory evidence, the possibility of the rat acting as an agent in the transmission of Lept. canicola infection must not be disregarded.

SUMMARY AND CONCLUSIONS

A series of 228 cases of leptospiral infections reported in the United States literature is reviewed. In comparison with the incidence in Europe and Great Britain, this total seems disproportionately low. The discrepancy appears to indicate diagnostic failure, probably due to a lack of awareness by American physicians of the clinical, epidemiologic and laboratory aspects of these infections. Even though the 78 cases of the Detroit area, reviewed in this paper, represent the largest single series ever reported in the United States, and despite greater availability of specific laboratory facilities in this area, the factor of diagnostic failure still obtained.

The Detroit survey revealed a number of additional factors. The role of rats and dogs in the transmission of these diseases, previously observed and recorded, was confirmed and emphasized. However, certain other aspects of leptospiral infections were revealed by this survey as important factors. It was indicated that in certain cases differential diagnosis of Lept. icterohaemorrhagiae and Lept. canicola was impossible unless repeated serologic tests are accomplished. In another group of cases involving only Lept. canicola the exclusive role of the dog as a transmission factor was questioned.

Detroit Department of Health.

29. Walch-Sorgdrager.[14] Meyer and others.[23]

A SYRINGE-TRANSMITTED EPIDEMIC OF INFECTIOUS HEPATITIS

With Observations Regarding the Incidence and Nature of Infectious Donors

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The danger of accidentally transmitting disease from one person to another by means of a common hypodermic syringe has generally been looked on as remote. This is particularly true when dealing with apparently healthy persons. In fact, until recently, syphilis and malaria were the only common infections which were known to be readily transmitted in this manner. With the widespread and frequent use of syringes in the modern practice of medicine, the demonstration that another disease, virus hepatitis, may be so transmitted becomes a matter of considerable importance.

It has now been experimentally demonstrated that virus hepatitis, including both the infectious or epidemic and the homologous serum type, may be transmitted to human beings by the parenteral injection of infected serum.[1] As little as 0.01 cc. of serum has been sufficient to produce the disease.[2] The filterable agent is present in the blood during both the prodromic and the acute stage of the illness and, in the case of homologous serum hepatitis, during the incubation period.[3] Accidental transmission through transfusions of whole blood, plasma and convalescent serum and injections of biologicals to which serum has been added has been frequently reported.[4] Less widely appreciated in this country is the danger of transmission by means of unsterile syringes or needles. British workers have shown that this frequently occurs [5] and can be prevented by proper sterilization.[5b,f] Transmission may also occur during an ordinary venipuncture for the withdrawal of blood, as well as during parenteral injections, since Mendelssohn and Witts [6] have demonstrated that

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In this investigation Drs. J. J. Kane, Robert N. Armen, Morris Rackenmacher and Irving Madoff gave valuable assistance.

1. (*a*) Oliphant, J. W.: Jaundice Following Administration of Human Serum, in Harvey Lectures, 1943-1944, Lancaster, Pa., Science Press, 1944, vol. 39, p. 254. (*b*) Paul, J. R.; Havens, W. P., Jr.; Sabin, A. B., and Philip, C. B.: Transmission Experiments in Serum Jaundice and Infectious Hepatitis, J. A. M. A. **128**: 911 (July 28) 1945. (*c*) Neefe, J. R.; Stokes, J., Jr.; Reinhold, J. G., and Lukens, F. D. W.: Hepatitis Due to the Injection of Homologous Blood Products in Human Volunteers, J. Clin. Investigation **23**: 836, 1944. (*d*) Findlay, G. M.; Martin, N. H., and Mitchell, J. B.: Hepatitis After Yellow Fever Inoculations: Relation to Infective Hepatitis, Lancet **2**: 301, 340 and 365, 1944.

2. Havens, W. P., Jr.: Period of Infectivity of Patients with Experimentally Induced Infectious Hepatitis, J. Exper. Med. **83**: 251, 1946.

3. Neefe, J. R.; Gellis, S. S., and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis, Am. J. Med. **1**: 3, 1946.

4. (*a*) Oliphant.[1a] (*b*) Findlay, Martin and Mitchell.[1d] (*c*) Murphy, H. M.: Transmission of Infectious Hepatitis by Blood Transfusion, Gastroenterology **5**: 449, 1945. (*d*) Rappaport, E. M.: Hepatitis Following Blood or Plasma Transfusions, J. A. M. A. **128**: 932 (July 28) 1945. (*e*) Grossman, S.: Homologous Serum Jaundice Following Administration of Commercial Pooled Plasma, New England J. Med. **234**: 181, 1946. (*f*) Beesan, P. B.; Chesney, G., and McFarlan, A. M.: Hepatitis Following Injection of Mumps Convalescent Plasma, Lancet **1**: 814, 1944. (*g*) Bradley, W. H.; Loutit, J. F., and Maunsell, K.: An Episode of Homologous Serum Jaundice, Brit. M. J. **2**: 268, 1944. (*h*) Sawyer, W. A.; Meyer, K. F.; Eaton, M. D.; Bauer, J. H.; Putnam, P., and Schwentker, F. F.: Jaundice in Army Personnel in the Western Region of the United States and Its Relation to Vaccination Against Yellow Fever, Am. J. Hyg. **39**: 337, 1944; **40**: 35, 1944.

5. (*a*) Bigger, J. W.: Jaundice in Syphilitics Under Treatment, Lancet **1**: 457, 1943. (*b*) Salaman, M. H.; King, A. J.; Williams, D. I., and Nicol, C. S.: Prevention of Jaundice Resulting from Anti-Syphilitic Treatment, ibid. **2**: 7, 1944. (*c*) Sheehan, H. L.: Epidemiology of Infective Hepatitis, ibid. **2**: 8, 1944. (*d*) Hartfall, S. J.: Jaundice in Rheumatoid Arthritis, ibid. **2**: 358, 1944. (*e*) Beattie, J., and Marshall, J.: The Aetiology of Post-Arsphenamine Jaundice, Brit. M. J. **1**: 547, 1944. (*f*) Loutit, J. F., and Maunsell, K.: Prevention of Homologous Serum Jaundice, ibid. **2**: 759, 1945. (*g*) Droller, H.: Outbreak of Hepatitis in a Diabetic Clinic, ibid. **1**: 623, 1945. (*h*) Darmady, E. M., and Hardwick, C.: Syringe Transmitted Hepatitis, Lancet **2**: 106, 1945. (*i*) Syringes, Serum and Jaundice, editorial, Brit. M. J. **1**: 810, 1945. (*j*) Role of Syringes in the Transmission of Jaundice, Memorandum by Medical Officers of the Ministry of Health, Lancet **2**: 116, 1945. (*k*) Syringe Transmitted Hepatitis, editorial, J. A. M. A. **129**: 278 (Sept. 22) 1945.

6. Mendelssohn, K., and Witts, L. J.: Transmission of Infection During Withdrawal of Blood, Brit. M. J. **1**: 625, 1945.

regurgitation of blood back into the vein usually occurs when the tourniquet is released. Finally, transmission by means of the "multiple dose per syringe" technic has been described.[7] In this method, which is commonly employed for the administration of such medicaments as vaccines, penicillin or antisyphilitic drugs to large groups, a small amount of serum is often unwittingly aspirated when the plunger is withdrawn to ascertain that the needle is not in a vein. In this manner the remaining material in the syringe may become infected.

Obviously the question of "carriers," or infectious donors of this disease, and the extent of their dissemination among the population is of fundamental importance in evaluating the danger of accidental parenteral transmission. During a special study of the problem of virus hepatitis conducted for the Surgeon General's Office by one of us (R. B. C.) at a United States Army General Hospital in this country, a syringe-transmitted epidemic of infectious hepatitis was encountered. A number of cases developed among men who had received tetanus toxoid on a certain day by the "multiple dose per syringe" technic. Since all the involved personnel who were available were studied, data regarding possible donors was obtained. We are making this report with this problem particularly in mind.

METHODS

Histories, physical examinations and the clinical portion of hepatic function tests were carried out in the clinic by a team of medical officers with special experience on the hepatitis wards. Patients with active hepatitis were admitted to the hospital and studied in detail.

The following laboratory procedures were employed. Retention of sulfobromophthalein sodium was determined at forty-five and sixty minutes after a dose of 5 mg. per kilogram. Previous control studies by ourselves and others [8] indicate that in this age group there should be no retention of dye even at forty-five minutes. For technical reasons we believe that 3 per cent and 2 per cent retention of dye at forty-five and sixty minutes respectively can be considered as doubtful and 4 per cent and 3 per cent as definitely abnormal. Serum bilirubin was determined spectrophotometrically, the modification of the Van den Bergh test described by Ducci and Watson being used.[9] Normal values according to Watson are 0.2 mg. per hundred cubic centimeters for the prompt direct (or one minute) reading of bilirubin and up to 0.8 mg. per hundred cubic centimeters for the total bilirubin. Ninety-seven per cent of our 35 normal controls gave values for both types of determination within this range. One case fell in the borderline range of 0.2 to 0.4 mg. per hundred cubic centimeters for the prompt direct reading. Urine urobilinogen was determined on a two hour specimen of urine by the quantitative method recently described by Watson, Schwartz, Sborov and Bertie.[10] Our control data indicate that the normal range originally proposed is probably too low. We feel that it is safer to take 1.0 to 1.5 total Ehrlich units as the borderline level and more than 1.5 total Ehrlich units as positive. Cholesterol esters were determined by Block's modification of Bloor's method.[11] All of our normal control determinations (15 cases) showed over 50 per cent esters, and 80 per cent of the controls showed over 55 per cent esters. Consequently, we have taken 50 to 55 per cent as borderline and less than 50 per cent as positive. Bilirubinuria was determined by the modified methylene blue test [12] and the "strip" test.[13] The cephalin cholesterol flocculation test was performed as described by Hanger.[14] It should be noted that our antigen was relatively insensitive, frequently giving negative results even during acute hepatitis with jaundice.

DESCRIPTION OF EPIDEMIC

One hundred and ten presumably healthy men, members of the detachment, received routine intramuscular injections in the arm of tetanus toxoid on Aug. 31, 1945. The material was administered from 10 cc. syringes containing ten doses each, and needles were changed between patients. A total of eleven syringes were required. Syringes were sterilized after being used for ten injections and before being refilled, while a freshly sterilized needle was employed for each patient. Sterilization was accomplished by means of a hot water sterilizer and was probably adequate, since enough equipment was available to allow for thirty minutes or more of immersion in boiling water.

Toward the end of September several cases of infectious hepatitis were recognized among the detachment, and inquiry revealed that in each case tetanus toxoid had been received on August 31. Consequently, all who had received toxoid on that date were called in for a history and a physical examination. Fifty-six men of the original 110 remained on the post, the others having been discharged or transferred elsewhere. Those with a history of acute symptoms or with abnormal physical findings compatible with infectious hepatitis were given a series of hepatic function tests. The examinations were done the second week of October, but unfortunately it was impossible to complete the laboratory part of the program until the first week of November. In consequence, abnormal findings in the cases of milder disease may have disappeared.

As indicated in table 1, history revealed that in 23 men symptoms developed characteristic of acute infectious hepatitis between September 15 and October 8. Specifically, the incubation period varied from twenty-one to thirty-eight days in 21 cases and was fifteen and sixteen days, respectively, in the other 2. Although the latter two intervals are unusually short, Havens has observed such incubation periods in artificially induced cases.[15] Two men gave a history of symptoms compatible with chronic hepatitis of six and nine months' duration, respectively, but neither had been sufficiently ill to report to sick call. The remaining 31 men denied the presence of symptoms during the previous two months.

7. Howells, L., and Kerr, J. D. O.: Hepatitis After Penicillin Injections, Lancet **2**: 51, 1946.

8. (*a*) Mateer, J. G.; Baltz, J. T.; Marion, D. F., and MacMillan, J. M.: Liver Function Tests, J. A. M. A. **121**: 723 (March 6) 1943. (*b*) Barker, M. H.; Capps, R. B., and Allen, F. W.: Chronic Hepatitis in the Mediterranean Theater, ibid. **129**: 653 (Nov. 3) 1945.

9. Ducci, H., and Watson, C. J.: The Quantitative Determination of the Serum Bilirubin with Special Reference to the Prompt Reacting and the Chloroform Soluble Types, J. Lab. & Clin. Med. **30**: 293, 1945.

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13. Hawkinson, V.; Watson, C. J., and Turner, R. H.: A Modification of Harrison's Test for Bilirubin in the Urine Especially Suited for Mass and Serial Usage, J. A. M. A. **129**: 514 (Oct. 13) 1945.

14. Hanger, F. M.: Serological Differentiation of Obstructive from Hepatogenous Jaundice by Flocculation of Cephalin Cholesterol Emulsions, J. Clin. Investigation **18**: 261, 1939.

15. Havens, W. P., Jr.: Immunity in Experimentally Induced Infectious Hepatitis, J. Exper. Med. **84**: 403, 1946.

TABLE 1.—*Occurrence of Acute Symptoms Consistent with Infectious Hepatitis Fifteen to Thirty-Eight Days After Injections of Toxoid*

	No. of Men
No recent symptoms	31
Chronic symptoms	2
Recent acute symptoms	23
Total men examined	56
Men that had left post	54
Total men receiving injections on August 31	110

RESULTS OF EXAMINATION OF INVOLVED PERSONNEL

The men in the group with acute symptoms gave a history of fatigue, indigestion especially to fatty foods, anorexia, flatulence and loose stools without real diarrhea. A few had nausea and vomiting, ache in the right upper quadrant, somnolence and urticaria. Fever was noted infrequently. In all cases symptoms persisted for at least ten days and usually longer. In a few instances aggravation from exercise was noted.[12b] One man (case 6) had dark urine and light stools.

The physical and laboratory observations in the group with acute symptoms are recorded in detail in table 2 Our evaluation of the significance of these observations is indicated by a division of cases into positive, questionable and negative or incomplete. In the "positive" group are placed all cases with either definite enlargement and tenderness of the liver, elevation of the retention of sulfobromophthalein sodium, increased serum bilirubin or multiple other abnormal findings. Cases in the "questionable" group all have evidence of hepatic dysfunction but less pronounced in degree. Findings in the last group are for the most part incomplete or negative. No laboratory tests at all were made in 3 of these cases.

All sulfobromophthalein sodium tests were done between October 24 and October 30 except for case 2, in which it was done on November 2, and case 6 on October 20. The Van den Bergh and other tests were performed between October 26 and November 9 except for case 10, in which they were done during the first two weeks of October. Clinical jaundice was observed only once (case 10). Likewise, bilirubinuria was found only in this 1 case, although a history of dark urine was not infrequently obtained. In the remaining patients, the disease must be classified as nonicteric or subclinical and therefore mild. Laboratory findings have frequently returned to normal in this type of case after three to six weeks.[16] This is particularly true of bilirubinuria and bilirubinemia, as well as the results of the cephalin cholesterol flocculation test. The significance of the negative results of the last test was further diminished by a relatively insensitive antigen. Finally, it should be noted that the subsequent disappearance of abnormal findings in many of our cases enhances their significance.

Unfortunately, it was impossible to make a similar set of observations on a control group due to lack of facilities. However, only 1 sporadic case of acute infectious hepatitis was recognized in the remainder of the detachment of approximately 700 men during the months of September and October, although the medical officers were alert for the disease. In view of the fact that 5 of our group of 23 men with acute symptoms reported to sick call voluntarily and were hospitalized, it appears extremely unlikely that the acute disease was epidemic in the rest of the detachment. It should further be noted that our laboratory procedures were individually con-

16. Barker, Capps and Allen.[12b] Neefe, J. R., and Reinhold, J. G.: Laboratory Aids in the Diagnosis and Management of Infectious (Epidemic) Hepatitis, Gastroenterology **7**: 393, 1946.

TABLE 2.—*Findings in All Men Having Symptoms Following Injection of Tetanus Toxoid on August 31* *

	Case No.	Onset of Symptoms	Liver: Fingers Below Costal Margin	Liver: Tenderness	Percentage Sulfobromophthalein in Retention, 45 Min./60 Min.	Bilirubin, Mg./100 Cc. Direct/Total	Urobilinogen, 2 Hr. T.E.U.†	Cholesterol Esters, Percentage	Cephalin Cholesterol Flocculation, 24/48 Hr.
Positive									
	1	10/ 5	2	0	4/0	0.23/1.18	1.32	31	...
	2	9/21	3	2+	0/0	0.31/?	....	60	0/1
	3	10/ 1	7	2+	8/5	0.1/0.3	1.51	45	0/0
	4‡	10/ 1	0	2+	7/5	0.1/0.3	1.09	33	...
	5§	10/ 1	0	0	22/13	0/0.41	1.58	46	0/0
	6‖	9/27	5	3+	2/0	0/0.3	1.16	..	0/1
	7	10/ 8	2	1+	5/4	.....	....	..	0/0
	8#	10/ 3	5	2+	0/0	0/0.17	....	39	0/1
	9	10/ 4	3	1+	3/2.5	0.03/1.18	1.18	57	...
	10	9/16	3	2+	...	5.7/8.0	8.20	36	1/3
	11	10/ 4	0	0	8/4	0.03/0.3	0.46	57	0/0
Questionable									
	12	10/ 6	0	0	4/2.5	.....	....	..	...
	13	10/ 3	2	0	0/0	0.1/1.0	1.40	61	0/0
	14	10/ 5	1	1+	0/0	0/0.1	0.90	41	0/0
	15	10/ 4	?	2+	0/0	0/0.17	1.40	42	0/0
	16	10/ 7	0	0	3/2	0.1/0.44	....	..	0/0
	17	9/25	0	0	3/3	0/0.23	0.38	49	0/0
Negative or incomplete									
	18	10/ 4	1	1+	3/0	0/0.38	1.27	..	0/0
	19	9/28	0	0	0/0	0.03/0.44	....	53	0/1
	20	9/15	0	0	...	.....	....	..	...
	21	9/25	0	0	...	.....	....	..	...
	22	10/ 8	0	2+	...	.....	....	..	...
	23	10/ 6	0	0	0/0	.....	1.80	..	0/1
Chronic									
	1 c	March	4	3+	3/0	0.23/0.52	4.50	40	1/2
	2 c	January	2	0	5/3	0.16/0.55	3.2	59	0/0
Asymptomatic									
	1 a	None	3	1+	4/3	.....	....	..	...
	2 a	None	2	0	2/1	.....	....	..	...
	3 a	None	2	0	0/0	0.06/0.23	2.55	59	...

* The table also includes observations on 2 patients with chronic hepatitis and 3 asymptomatic patients with large livers.
† Total Ehrlich units.
‡ Four weeks later retention of sulfobromophthalein was 1/0 and the percentage of cholesterol esters was 61.
§ Five weeks later the liver extended 6 cm. below the costal margin.
‖ At the onset there were urticaria, light stools and aggravation from exertion.
There was aggravation of symptoms from exertion.

trolled, detachment personnel and patients being used as indicated in the section on methods. The figures so obtained were used to establish our normal values and so constitute a partial control.

There was no segregation of the group studied as compared with the rest of the detachment in regard to living quarters, duty assignments or mess. Since the toxoid injection was the only apparent common factor, it is evident that it must have had etiologic significance. In view of these facts it is not unlikely that all 23 men who experienced similar acute symptoms at an appropriate interval following presumed exposure actually had acute infectious hepatitis. However, even in an epidemic in which clearcut cases with jaundice are present it is best to require objective evidence of hepatic abnormality before making the diagnosis of hepatitis. On this basis there were 11 definite cases ("positive" group, table 3) with perhaps 6 more doubtful ones ("questionable" group, table 3).

TABLE 3.—*Summary of Physical and Laboratory Findings in Men in Whom Acute Symptoms Developed in Fifteen to Thirty-Eight Days After Injections* *

Physical and Laboratory Findings	Number of Cases	Percentage of Total Examined
Definitely diagnostic of hepatitis	11	19.6
Questionably diagnostic of hepatitis	6	10.7
Negative or incomplete	6	10.7
Total men with acute symptoms	23	41.0

* Complete findings are recorded in table 2.

Examination of the 2 patients with chronic symptoms revealed that both had physical and laboratory evidence of hepatic disease without jaundice (table 2). One gave a history of having accidently swallowed serum from a patient suspected of infectious hepatitis while working as a laboratory technician late in July. An exacerbation of his symptoms occurred on September 10. The nature of the hepatic disease in this case is not clear. It may have been a chronic infectious hepatitis with a superimposed acute infection possibly from another strain, or it may have been either one alone. In any case he did not contract his disease on August 31 but on the contrary was possibly infectious at that time and may have served as one of the donors.

Physical examination of the 31 men without symptoms revealed 3 with enlarged livers, one being slightly tender. Unfortunately it was not feasible to do further tests on any but these 3. As shown in table 2 (cases 1a, 2a, and 3a under "asymptomatic") 1 had a definitely elevated retention of sulfobromophthalein sodium and 1 an increased excretion of urobilinogen. Whether these cases represent asymptomatic acute infectious hepatitis, chronic asymptomatic (inactive) infectious hepatitis or some other type of hepatic disease cannot be stated. Possibly some were infectious. If all 31 asymptomatic men had been given hepatic function tests, probably more cases of this sort would have been discovered.

THE INCIDENCE OF DONORS OR "CARRIERS"

Eleven of the 56 men who were examined had contracted acute infectious hepatitis, an incidence of 20 per cent. This makes it probable that of the original 110 men given injections, approximately 22 contracted the disease. Since a maximum of 9 men could have been infected from a single syringe, assuming in each instance that the first person given an injection was a donor, it follows that there must have been at least three contaminated syringes and 3 infectious donors. However, it is more likely that on the average a syringe would become contaminated when half empty, so that only 4 or 5 men would be exposed per contaminated syringe. If the more conservative figure is employed, there would have been five such syringes or 5 infectious donors, making an incidence of 5 per cent in the original group (table 4).

TABLE 4.—*Showing Derivation of the Probable Incidence of Infected Donors in Original Group*

Total number of men receiving injections August 31	110
Percentage contracting acute infectious hepatitis	20
Total number of original group contracting hepatitis	22
Number of infected syringes (average of 5 men infected per syringe)	5
Percentage of "donors" in original group	5

Although these figures are too small to justify accurate statistical analysis, most of the potential errors would lead to a higher incidence of donors. Thus, as previously pointed out, the number of men contracting acute hepatitis was probably greater than 20 per cent. Secondly, it is unlikely that serum would be aspirated from every infectious person. And finally, 25 to 50 per cent of persons given injections of infectious material do not contract the disease, presumably because of immunity.[17] Consequently, it can be concluded that the incidence of infectious donors or carriers in the original group was probably at least 5 per cent and possibly much higher.

There is, of course, no way of ascertaining which men acted as infectious donors. Information is not available regarding the 54 men who had left the post except that there was no record of any of these having reported to sick call. One who left about the middle of September may have been jaundiced. He was observed by a medical officer during a casual meeting at the time of his departure. The only conclusion to be drawn is that the infectious donors were either asymptomatic or not sufficiently ill voluntarily to report to sick call. It seems probable that some of them fell into the first group and were apparently healthy. Whether such donors are true carriers or represent asymptomatic cases of acute or chronic infectious hepatitis recognizable only by laboratory procedures cannot be determined from this data.

COMMENT

This study demonstrates in a striking manner the danger of extensive dissemination of the virus of infectious hepatitis through the use of the "multiple dose per syringe" technic. That this was the actual mode of transmission cannot, of course, be absolutely proved, but it appears to be the only reasonable explanation. Sterilization of needles and syringes before and after use was apparently adequate. Furthermore, in the absence of gross carelessness, improper sterilization could hardly account for the large number of cases observed. In evaluating the high incidence of induced infection, 20 per cent, it is well to remember that the cases of mild nonicteric infectious hepatitis are difficult to diagnose and are usually not recognized except during an epidemic when the date of exposure is known. These persons often fail to consult a physician because symptoms are not sufficiently severe. Thus

17. (*a*) Havens.[18] (*b*) Neefe, J. R.: Recent Advances in the Knowledge of "Virus Hepatitis," M. Clin. North America **30**: 1407, 1946.

in our group only 1 man had clinical jaundice and probably not over one third would have voluntarily reported to sick call. It is recognized that some may differ with our criteria for making the diagnosis of acute hepatitis without jaundice. Although we agree that it is a particularly difficult diagnosis in sporadic cases, in an epidemic of this sort when the date of exposure is known we believe that it can be made with reasonable assurance.

Of unusual interest is the rather surprising inference that approximately 5 per cent and possibly more of an unselected group of 110 men carried the virus of infectious hepatitis in their blood. Only 20 per cent of those questioned had been overseas and none had been in the Mediterranean theater, where the incidence of hepatitis was greatest. No explanation for this high figure is available.

Judging from the short incubation period, this epidemic was one of so-called epidemic hepatitis. It is of interest that Sawyer and co-workers [4b] in a careful study of the homologous serum epidemic of 1942 in the army arrived at a similar figure for the incidence of carriers. They suggested that 6 per cent and probably considerably more of the population carry this virus in their blood. This figure was based on the assumption that forty-seven lots of yellow fever vaccine out of a total of one hundred and seventeen studied were infected or icterogenic. To each lot was added pooled plasma from known donors. Nine hundred and seventy different donors were used, affording a fair sample of the local population. However, there is reason to suspect that more than forty-seven lots of vaccine were icterogenic and that a 6 per cent incidence of carriers is consequently too low. Thus the incidence of hepatitis from each lot of vaccine was determined by questionnaire and undoubtedly included only hospitalized patients. A careful study of unselected samples of both hospitalized and ambulatory recipients of two lots of vaccine at Fort Custer by one of us (R. B. C.) in association with others [18] gave startlingly different results, as shown in table 5. Lot 368 was generally admitted to be icterogenic but lot 382 was classified as nonicterogenic by Sawyer. Similar studies involving four other lots of vaccine classified as nonicterogenic were made at Fort Custer. The groups were too small for statistical analysis, but the trend was the same as for lot 382. Most of the cases occurring after use of these lots were mild, either nonicteric or with only a slight, transitory jaundice and would never have been recognized unless unselected samples of ambulatory recipients had been studied. From this data we can conclude that probably considerably more than forty-seven lots contained the virus and that the incidence of carriers was correspondingly higher than 6 per cent.

TABLE 5.—*Incidence of Hepatitis Per Thousand Men Given Injections from Two Different Lots of Yellow Fever Vaccine*

Vaccine Lot No.	Sawyer et Al.[4b]	Custer [18]	Size of Custer Sample
368	67.59	371.0	1,857
382	0.33	220.0	146

Finally, the wide dissemination of this virus among the population is evidenced by the frequency of catarrhal jaundice, which is probably identical with what is now called infectious or epidemic hepatitis. It is generally stated that approximately 5 per cent of adults give a history of this disease. If we also include the cases of unrecognized nonicteric disease, the total incidence would probably be at least 10 to 15 per cent and possibly considerably higher.

The few experimental observations available on human volunteers have failed to demonstrate persistence of the virus in the blood stream after the first month of illness,[19] although Neefe and co-workers have recently shown that the virus may persist in the feces and liver.[19c] However, it is difficult to explain the evidence presented in this paper except by the assumption that some persons become "carriers" of the virus, which is present in their blood. Since there is no way of determining which of our patients actually served as infectious donors, definite conclusions regarding the nature of such carriers cannot be reached. It can, however, be stated that only 2 of the potential carriers had symptoms and that in neither case were the symptoms sufficiently severe to require professional advice. Furthermore, none had a history of jaundice. Thus, for practical purposes, carriers may be apparently healthy persons without a recognizable past history of hepatic disease. Presumably their original infection was of the mild nonicteric type which is probably the most common. Whether persons with chronic symptomatic (or active) hepatitis or with asymptomatic evidence of hepatic disease (inactive hepatitis) are more likely to be carriers than those without any residuals is not known.

Sawyer and his colleagues [4b] arrived at essentially the same conclusions in their study of the plasma donors responsible for the homologous serum epidemic of 1942. In the case of many of the lots of icterogenic vaccine there were no donors with a history of jaundice, while in others there were donors with a history of jaundice from one to twenty years previously. In most cases donors were apparently well at the time of the blood letting.

The foregoing considerations have an important bearing on the potential danger of accidently transmitting this disease by parenteral inoculation. Not only does the available evidence indicate a relatively high incidence of carriers in the population but the nature of the latter is such that detection is for practical purposes impossible. Thus in the use of blood and blood products a calculated risk must be assumed. Syringe and needle technics should be carefully checked and revised, so that proper sterilization is accomplished. Consideration should also be given to the technic of finger puncture for blood counts. Although cases produced in this way have not yet been observed, there can be no doubt that the usual methods do not provide satisfactory sterilization of needles or lancets.

These observations reemphasize the frequency of acute hepatitis without jaundice. In this group 91 per cent of the cases fell into this category. In a previous study of the homologous serum epidemic of 1942 we reported that 70 per cent of 1,958 cases were without

18. Report to the Surgeon General's Office of a Special Board for the Investigation of Jaundice at Fort Custer, Mich., 1942. Other members were Lieut. Col. M. H. Barker, Medical Corps, Major K. F. Bennet, Medical Corps, Major A. E. De Groat, Medical Corps, Major H. A. Davenport, Medical Corps, and Major F. W. Fitz, Medical Corps.

19. (*a*) Havens.[3] (*b*) Neefe.[17b] (*c*) Neefe, J. R.; Stokes, J. Jr.; Garber, R. S., and Gellis, S. S.: Studies on the Relationship of Hepatitis Virus to Persistent Symptoms, Disability and Hepatic Disturbance Following Acute Infectious Hepatitis. J. Clin. Investigation **26**: 329, 1947.

jaundice.[15b] Among the 32 cases studied from vaccine lot 382 (table 5), 90 per cent were nonicteric. On the other hand, in an epidemic studied by Neefe [15b] in only 26 per cent of 342 cases did overt jaundice fail to develop. Such variations are to be expected. Nevertheless, it is obvious that the nonicteric form of the disease is common.

It is noteworthy that 4 of the 10 persons with nonicteric disease were still sick three months after onset and could be classified as entering the chronic stage.[8b] This lends support to the concept proposed by Bloomfield in 1938 [20] and previously supported by ourselves [6b] that acute nonicteric hepatitis may lead to chronic hepatitis and perhaps in some cases to cirrhosis. This possibility is undoubtedly enhanced by lack of treatment resulting from failure to make the diagnosis. The importance of proper recognition is obvious.

CONCLUSIONS

An outbreak of infectious hepatitis apparently resulting from the use of the "multiple dose per syringe" technic for the administration of tetanus toxoid is reported. At least 20 per cent of the recipients of the toxoid contracted acute infectious hepatitis. It is estimated that probably 5 per cent of the original group must have carried the virus in their blood. Most of these were apparently asymptomatic and none were sufficiently ill to consult a physician voluntarily. The epidemiologic import of these figures is discussed, particularly as involves transmission by way of plasma, blood and syringe.

EPITHELIAL METAPLASIA OF THE URINARY TRACT

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The finding of tissue cells of another type than those normally found in an organ of the body is always intriguing, and the explanation of such an occurrence presents many difficulties. It is not strange that differences of opinion have arisen as to the exact mechanism by which such a metamorphosis of tissue cells has been produced.

Such changes are found not infrequently in the epithelium of the urinary tract, where they present an interesting urologic study. In this discussion I am confining my attention to the changes occurring in the renal pelvis, the ureters and the bladder. Although the epithelium of these organs possesses a different derivation embryologically, that of the ureter and pelvis being mesodermal and that of the bladder partly entodermal and partly mesodermal, they are all lined with transitional cell epithelium, and, except perhaps in the immediate neighborhood of the bladder outlet, true glands are not normally present.

Metamorphosis of the epithelium in these organs is of two distinct types: 1. The substitution for the normal transitional cell epithelium of a stratified keratinizing epithelium and the development of leukoplakia and, by what may be regarded as a further extension of the process, squamous cell carcinoma. In this group, the epithelial change is toward an epidermal type of cell. 2. The appearance in the mucosa of glandular formations, with secretory properties, the so-called cystitis glandularis. In a striking parallelism to the preceding group, there develops a mucin-secreting adenocarcinoma. In this group, the change is toward an entodermal type in which an epithelium is found, resembling that of the large bowel.

Though various explanations have been advanced to explain these processes, two theories are most widely held at the present time: (1) that the changes are due to embryonic cell inclusions from contiguous structures; particularly is this a point of conflict of opinion in the matter of the glandular formations; (2) that the changes are due to metaplasia.

It is desirable that the two groups be considered separately, even if there are many instances of significant parallelism in their respective courses. In some conditions in which they are commonly encountered, notably in exstrophy of the bladder and in the bladders of sufferers from schistosomiasis, they are found in intimate association.

The literature is rather voluminous, and I shall not attempt to cover it. At times it is even repetitious, a fault of which I myself may on this occasion be found guilty.

It is necessary to consider, on the one hand, leukoplakia and squamous cell carcinoma and, on the other hand, cystitis glandularis and the mucin-secreting adenocarcinoma.

LEUKOPLAKIA AND SQUAMOUS CELL CARCINOMA

Since 1900, up to which time few cases of leukoplakia and squamous cell carcinoma had been reported, there has been a steady increase in the number of case reports appearing in the literature, so much so that neither may be regarded as an unduly rare occurrence. It is perhaps reasonable that leukoplakia is noted less frequently than the more serious squamous cell carcinoma. Both conditions are met with most often in the bladder, less so in the renal pelvis and least of all in the ureters. They may even be observed in multiple foci.

There is not the same tendency to ascribe the presence of leukoplakia to embryonic cell inclusions as in the case of the glandular formations. Though some authors, in particular Hinman and Gibson,[1] have explained its occurrence as the result of an effort on the part of the epithelium to exercise its inherent power of adaptation to environment in the form of protective cornification, most authors, including the pathologists, have agreed that leukoplakia is metaplasic in origin.

Leukoplakia is usually associated with long-standing irritation and inflammation. It also follows, as has been shown by Wolbach and Rowe [2] experimentally the deprivation of fat-soluble vitamin A in laboratory animals. They showed that many different types of epithelium were replaced by stratified keratinizing epithelium, not only in the genitourinary tract, but also in the gallbladder, the trachea and the eyes. In their article, the autopsy of a case occurring in a human being was reported, in which the same epithelial changes were observed. In a later article, the same authors showed that no matter what type of epithelium was involved, in spite of origin from any of the three embryonic layers, in the repair following restoration of the diet, each epithelium was replaced by the kind

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Address of the invited foreign guest read before the Section on Urology at the Ninety-Sixth Annual Session of the American Medical Association, Atlantic City, N. J., June 12, 1947.

20. Bloomfield, A. L.: The Natural History of Chronic Hepatitis, Am. J. M. Sc. 196: 429, 1938.

1. Hinman, F., and Gibson, T. E.: J. Urol. 6: 1, 1921.

2. Wolbach, S. B., and Rowe, P. R.: J. Exper. Med. 42: 753, 1925; Vitamin A Deficiency in Guinea Pig, Arch. Path. 5: 239 (Feb.) 1928; J. Exper. Med. 57: 511, 1933.

normal to the location. They stated their conviction that the occurrence of leukoplakia is due to metaplasia. They made a most significant observation when they stated that "the behavior of the cells in a few of the animals . . . suggests the acquisition of neoplastic properties."

Most authors look on leukoplakia as a precursor of squamous cell carcinoma and believe that the cancer is an extension of the process. Against this, it has been urged that not all cancers are preceded by leukoplakia. Further than this is the fact that in only a relatively small number of cases have leukoplakia and squamous cell carcinoma been found in association.

In 1929 I collected 13 cases in which the two conditions were associated.[3] Since that time eight other case reports have been made, 4 by Goebel,[4] a second by Scholl,[5] and 1 each by Potts,[6] Kilman [7] and Aschner.[8] Rabson in 1936,[9] collected 18 instances of their occurrence in the bladder.

The report of Goebel deserved more than a passing reference. This was based on a study of tumors of the bladder in schistosomiasis. He found that in 4.3 per cent of sufferers from this disease cancers of the bladder developed. Schrumpf-Pierron [10] stated that, although the incidence of malignant tumors in Egypt is ten times less than in Europe and on this continent, the incidence of cancers of the bladder is much higher relatively. About 13 per cent of malignant disease in Egypt is due to schistosomiasis, mainly in the bladder.

The infestation of the bladder with Schistosoma haematobium is accompanied by intense irritation and produces a condition most favorable for metaplasic changes. Goebel reported 20 cancers of the bladder of which 11 were squamous cell carcinoma. All of these cases showed associated epidermoid metaplasia, and in 4 there were definite leukoplakias. Incidentally, there was 1 case of glandular cancer in his series.

The fact that relatively so few instances of the association of the two conditions have been found has been cited against the belief of a causal relationship. However, several authors have demonstrated intermediate stages between the two processes. Hinman, Kutzman and Gibson [11] observed, in sections of leukoplakia of the renal pelvis, evidences of what they thought must be regarded as definitely precancerous lesions. Hallé,[12] in a case in which the leukoplakia and squamous cell carcinoma were associated, found definite intermediate steps between the two conditions. We ourselves were able to give some confirmation to this finding. In our reported case of associated leukoplakia and squamous cell carcinoma of the renal pelvis and bladder, my colleague, the late Dr. Rhea, by taking serial sections, was able to demonstrate evidences of a transition between the two conditions.[13] These, in his opinion, if not definitely malignant, were certainly precancerous.

It may be that the question is not one of paramount importance. It is not necessary to assume that squamous cell carcinoma must be preceded by leukoplakia. Rabson [9] suggested that it is probable that squamous cell carcinoma in the bladder is caused by the same factors responsible for the leukoplakia, and that the carcinoma represents a "further distortion and exaggeration of the metaplasic process." In these cases, there is no intermediate benign stage, but rather an acceleration of the metaplasic process and an uninterrupted development of the malignancy. The condition, in other words, is malignant from the outset.

CYSTITIS GLANDULARIS AND MUCIN-SECRETING ADENOCARCINOMAS

The occurrence in the bladder of glandular formations possessing the faculty of secreting mucin has given rise to much discussion, and diametrically opposed views are held as to their origin. Is the process a metaplasic one, the result of chronic irritation or inflammation, or is it the result of embryonic inclusions of germinal cells of the lower intestinal tract? In view of the partial derivation of the bladder epithelium from entodermal tissues and as the bladder normally is devoid of glands, this latter assumption was not entirely unnatural. Probably the earliest reports of what is now known as cystitis glandularis were made on the exstrophied bladder, and such an assumption must have appeared logical to its first observers. However, in recent years, several facts have been revealed which makes the metaplasic theory a much more plausible one.

There are the observations of Enderlen [14] and Formiggini.[15] Both authors noted that the mucosa of the exstrophied bladder at birth was normal and that it was lined with normal transitional cell epithelium. There was a complete absence of glandular formations. The leukoplakia and cystitis glandularis which are such prominent features of the exstrophied bladder must therefore be regarded as postnatal acquisitions.

Furthermore, the occurrence of glandular formations in the renal pelvis and ureter (pyelitis and ureteritis glandularis) has been reported, notably by Brütt [16] and Paschkis.[17] The occurrence of mucin-secreting adenocarcinomas in the renal pelvis and in the ureter has also been reported. As the epithelium in these organs is derived from mesodermal tissues, the theory of entodermal inclusion loses much of its force.

Stoerk and Zuckerkandl [18] were the first to suggest that the glandular formations developed from the epithelial cell nests of von Limbeck and von Brünn, as the result of chronic inflammation. They were convinced that the process was definitely a secretory one and not a degenerative one. In the epithelial cell nest a cavity develops, gradually becoming lined with characteristic tall cells, with basally placed nuclei. The end result is a gland which secretes mucin, a condition to which they gave the name of cystitis glandularis. They stated their conviction that the theory of the developmental origin of cystitis glandularis had lost every basis of fact.

3. Patch, F. S.: New England J. Med. **20**: 423, 1929.
4. Goebel, G.: Ztschr. f. Krebsforsch. **3**: 369, 1905.
5. Scholl, A. J.: Surg., Gynec. & Obst. **34**: 189, 1922; J. Urol. **44**: 739, 1940.
6. Potts, W. J.: Squamous Cell Carcinoma of Renal Pelvis Associated with Stone and Leukoplakia, Arch. Surg. **25**: 458 (Sept.) 1932.
7. Kilman, J. R., cited by Davidson.[3]
8. Aschner, P. W.: Surg., Gynec. & Obst. **35**: 749, 1922.
9. Rabson, S. M.: J. Urol. **35**: 321, 1936.
10. Schrumpf-Pierron, P.: Ztschr. f. Krebsforsch. **36**: 145, 1932.
11. Hinman, F.; Kutzman, A. A., and Gibson, T. E.: Surg., Gynec. & Obst. **34**: 473, 1924.
12. Hallé, N.: Ann. d. mal. de org. genito-urin. **14**: 481 and 577 1896.
13. Patch, F. S., and Rhea, L. J.: Canad. M. A. J. **33**: 597, 1935.
14. Enderlen: Verhandl. d. deutsch. path. Gesellsch., 1904, p. 167.
15. Formiggini, B.: Riforma med. **36**: 252, 1920; abstracted, J. de chir. **17**: 176, 1921.
16. Brutt, H.: Ztschr. f. urol. Chir. **14**: 157, 1924.
17. Paschkis, R.: Folia urol. **7**: 55, 1913.
18. Stoerk, D., and Zuckerkandl, O.: Ztschr. f. Urol. **1**: 1 and 153, 1907.

In the same article, these authors pointed out that it might well be expected that epithelium which had undergone such a deviation from its normal character and had developed the habit of proliferation would go further and acquire malignant properties. In support of this, they reported a case of mucinous adenocarcinoma which had developed in an exstrophied bladder.

Furthermore, the changes which I am describing have been produced experimentally. Giani,[19] in an experiment for another purpose, introduced foreign bodies into the bladder of a rabbit and was surprised to observe the development of epithelial cell nests and cystitis cystica.

At this point, it seems desirable to make a brief reference to the not infrequent finding of cystitis cystica and the corresponding conditions in the renal pelvis and ureter. It is my opinion that these conditions represent one aspect of the process, which ordinarily leads to the development of active glandular formations. If the stimulus which initiated the process of adaptation should become inert, the process may be retarded and the gland epithelium may cease to function, or perhaps, overdistended by their own secretions, the epithelial cells become flattened and atrophied, and an impotent cyst remains. In other words, the cystic formations may be regarded as mere by-products of the process.

Most textbooks on pathology and urology speak of adenocarcinomas of the urinary tract as being exceedingly rare. Yet when one reviews the literature more closely one finds a surprising number of reports.

1. *Renal Pelvis.*—Four cases in the renal pelvis have been reported, those of Paschkis, Grohé.[20] Plaut [21] and Ackerman.[22]

2. *Ureter.*—Seven cases in the ureter have been reported, by Metcalf and Safford,[23] Kneise,[24] and 5 cases cited by Scott [25] (Cross, Einzig, Harrah, Mayock and Baurys, and Papin).

3. *Bladder.*—Here, it is not easy to compile statistics partly owing to the confusion which exists in describing these tumors and the great variation which is found in their nomenclature. Further, frequently no reference is made to the question of secretion of mucin.

In any event, the tumor is relatively a rare one. Scholl [5] found 5 in 333 tumors of the bladder observed at the Mayo Clinic in ten years. One of these occurred in an exstrophied bladder. Gayet [26] found 21 cases of cancer in exstrophied bladders, 16 being adenocarcinomas and 2 of the squamous cell variety. In the Montreal General Hospital only 3 cases of mucinous adenocarcinomas have been observed since 1910.

Some confusion has arisen in connection with tumors of the bladder vault, which some authors claim are in reality urachal tumors presenting in the bladder. Begg [27] (1936) reported 5 colloid adenocarcinomas and 2 adenocarcinomas (not colloid) which he placed in this category. In addition to these, he found 14 colloid adenocarcinomas in the urachus and 1 adenocarcinoma (not colloid). Hayes and Segal [28] (1945) in reporting a case stated that they had found an additional 25 cases in the literature. Higgins [29] has reported a further case.

Without making an exhaustive and critical study of these cases, it would appear that some cases at least have been included as urachal tumors which were regarded by the authors as being definitely of vesical origin.

Doubtless some tumors in the bladder vault originate in urachal epithelium. It is not proved, however, that all of them do. Two of the 3 cases reported by us [30] were situated in this area of the bladder. That they were of vesical origin was proved by intraperitoneal observation. In our third case it was in the neighborhood of a ureteral orifice.

Begg,[27] who has shown a special interest in urachal tumors, admitted that the urachus is a modified upper end of the fetal bladder and that its epithelium is essentially similar to that of the bladder. He stated:

> The urachal cells retain all the potentialities of primitive cloacal cells and are able to bring them at any period of life to fruition. Complete, but ill-regulated development toward glandular or transitional epithelium respectively may be observed. This development may overstep all bounds and give rise to colloid adeno-carcinoma on the one hand or squamous cell carcinoma on the other. As a rule, the full impulse given by the entodermal origin of the cells predominates, and the formations commonly seen pass through the stages of simple adenoma and adeno-carcinoma to reach finally the fully-formed colloid cancer of the rectal type.

It seems, however, that the question of urachal origin is not of paramount importance, when one considers that the urachal epithelium is similar to that of the bladder. The theory that an adenocarcinoma arising in the urachus is due to embryonic cell inclusions is just as open to argument as in the case of one arising in the bladder, and the metaplasic hypothesis is equally plausible.

It is interesting to compare the incidence of cancer in the exstrophied bladder, and in the bladder infested with the S. haematobium. In both cases an intense and long-contained irritation is present. In both there is an increased incidence of malignant growths of both types.

In the exstrophied bladder, as has been pointed out, mucinous adenocarcinomas predominate, possibly the result of an effort of the epithelium to adapt itself to its environment and to prevent, by a profuse secretion of mucus, an excessive desiccation of the exposed vesical epithelium. In the bladder affected by schistosomiasis, however, the squamous cell carcinomas predominate, in almost inverse ratio. This may be regarded as an attempt of the vesical epithelium to adapt itself to its irritating environment by the development of a protective cornification.

In both conditions the vesical epithelium strives to adapt itself to its environment by utilizing both methods. So in the exstrophied bladder, leukoplakia is often found in close association with cystitis glandularis, while in the bladder affected by schistomosiasis the reverse obtains.

Except in these two conditions, it is not easy to form any conclusions on the association of cystitis glandularis and adenocarcinoma. Often the diagnosis is based on the sole examination of a surgical specimen. Autopsies which would permit the fullest examination of the

19. Giani, R.: Centralbl. f. allg. Path. u. path. Anat. **17**: 180 and 900, 1906; Beitr. z. path. Anat. u. z. allg. Path. **42**: 1, 1907.
20. Grohe, B.: Deutsche Ztschr. f. Chir. **60**: 1, 1901.
21. Plaut, A.: Ztschr. f. urol. Chir. **26**: 562, 1929.
22. Ackerman, L. V.: J. Urol. **55**: 36, 1946.
23. Metcalf, W. F., and Safford, W. E.: Am. J. M. Sc. **129**: 50, 1905.
24. Kneise, O.: Ztschr. f. Urol. **24**: 10, 1930.
25. Scott, W. W.: J. Urol. **50**: 45, 1944.
26. Gayet, R.: J. d'urol. **39**: 295, 1935.
27. Begg, R. C.: Brit. J. Surg. **18**: 422, 1931.
28. Hayes, J. J., and Segal, A. D.: J. Urol. **53**: 659, 1945.
29. Higgins, C. C.: Urol. & Cutan. Rev. **50**: 4, 1946.
30. Patch, F. S., and Pritchard, J. E.: J. Urol. **57**: 126, 1947.

urinary tract are not always secured. None the less, many authors have noted the finding of cystitis glandularis in close association with the carcinoma.

In view of the frequent occurrence of cystitis glandularis and its comparable conditions in the renal pelvis and ureter, that so few cases of adenocarcinoma develop is a fact not easy to explain. It may be reasonable to infer that in many cases the original inciting factor ceases to be active and that recovery follows. In this respect the disappearance of the leukoplakia in the previously cited experiments of Wolbach and Rowe is most significant.

It may be, as was suggested in the discussion of the relationship between leukoplakia and squamous cell carcinoma, that an adenocarcinoma may result from an acceleration of the metaplasic process, stimulated by the same conditions which produced in more leisurely fashion the benign glandular formations.

In this connection, it may be noted that clinical observations have shown that the cystic and glandular formations in the bladder, at least, may disappear when the inciting irritation or infection has been eradicated by appropriate measures.

Though no clinical observations on the disappearance of leukoplakia in the human being are found, the experimental work of Wolbach and Rowe has shown that this does occur in laboratory animals. In animals in which leukoplakia had developed when they were given a diet deficient in vitamin A, the leukoplakia completely disappeared once the animals were restored to a normal diet.

Epithelial cells of the urinary tract possess latent potentialities of proliferation which, even on minimal irritation, may be followed by further, even unrestrained, growth. This change in the character of the cell may cease to be active or may even be reversed.

In view of the many doubts which still exist regarding the character of the changes which I have been discussing and which I regard as metaplasic, it is highly desirable that every opportunity be used to make complete and thorough examinations in every case in which they are observed.

CONCLUSIONS

Leukoplakia of the renal pelvis, ureters and bladder, and cystitis (pyelitis and ureteritis) glandularis are the result of epithelial metaplasia in response to a call for altered function, or at least as the result of altered environment. These metaplasias are commonly associated with chronic, long-standing irritation or infection.

Leukoplakia may follow vitamin A deficiency. In this condition it is not secondary to an infection.

The extent and intensity of the metaplasic process is in direct relation to the intensity and duration of the inciting factors.

Both conditions are potentially malignant. They may develop a malignant character by a further extension of the metaplasic process into squamous cell carcinoma and mucinous adenocarcinoma respectively.

Both types of cancer may develop, primarily, by an acceleration or intensification of the metaplasic process. It is possible that the epithelial changes may be reversible.

Clinical Notes, Suggestions and New Instruments

PULMONARY AND CEREBRAL FAT EMBOLISM FOLLOWING INTRAVENOUS ADMINISTRATION OF ETHER THERAPEUTICALLY

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The administration of ether intravenously for the nonsurgical treatment of impending ischemic gangrene has recently been advocated [1] as a safe procedure that promotes collateral circulation and affords relief from severe pain. Specifically, the advocates of this method of treatment for peripheral vascular disease recommend the daily infusion of 2½ per cent ether in a liter of isotonic solution of sodium chloride or (for hypertensive patients) dextrose for twelve consecutive days, followed after two days rest by a second course. Some of the complications encountered in carrying out this regimen have already been pointed out by Wirtschafter and Widmann.[2] The purpose of this report is to direct attention to another serious complication. In the first case in which the method indicated was employed at this hospital,[3] a fatality ensued during the course of treatment, which autopsy showed to have resulted from fat embolism. Inasmuch as the therapeutic regimen in question is likely to be given a rather wide clinical trial, it seems timely to emphasize, without prejudice to whatever therapeutic efficacy it may possess, that the intravenous administration of ether may be potentially dangerous.

REPORT OF CASE

History.—The patient was a moderately obese, hypertensive Negress, 75 years of age, who three months previously had had her left fifth toe amputated because of infection, Staphylococcus aureus having been obtained on culture. At the time, the dorsalis pedis artery could not be palpated, nor did oscillometric readings show any evidence of pulsation of the vessels of the calf on either side. The blood pressure was 240 systolic and 130 diastolic. The Kahn and Kline reactions were negative. Two weeks after the operation the wound broke down and examination showed an ulcerated, infected area on the dorsum of the amputation stump, as well as some swelling of the foot. Inasmuch as the conventional conservative methods had not proved efficacious and the patient declined further surgical intervention, it was decided to institute intravenous ether therapy, following precisely the method advocated by Katz.[1] During the course of treatment, the wound did become smaller and better demarcated and there was some subjective improvement, manifested chiefly in diminution of pain in the foot. During the course of the fifteenth infusion, however, after the latter had been going for one and three-fourths hours, the patient had a shaking chill and a temperature of 104 F., associated with substernal pain, nausea and vomiting. It was noted also that the blood pressure had dropped sharply to 110 systolic and that the pulse rate had risen to 120. The respiratory rate subsequently rose to 50 and the pulse to 150, the latter being shallow and thready. During the following day, the patient complained of respiratory difficulty even while in an oxygen tent, and in spite of supportive measures she died about thirty-five hours after the onset of untoward symptoms.

Postmortem Examination.—The significant observations only will be indicated. At the site of the amputation there was a small granulating wound, about 1 cm. in diameter, through which a spicule of bone from the head of the metatarsal bone protruded. The surrounding soft parts of the stump, however, showed no evidence of recent infection. As for the viscera, the heart was appreciably hypertrophied, reflecting the hyper-

From the Laboratory Division, Hospital for Joint Diseases.

1. Katz, R. A.: Impending Ischemic Gangrene: New Non-Surgical Therapeutic Suggestions, New Orleans M. & S. J. 98: 542-554 (June) 1946.
2. Wirtschafter, Z. T., and Widmann, R.: The Elaboration of Histamine in Vivo in the Treatment of Peripheral Vascular Disorders: A Preliminary Report, J. A. M. A. 133: 604-605 (March 1) 1947.
3. On the Orthopedic Service of Dr. Harry D. Sonnenschein.

tension, and showed patches of old myocardial fibrosis in the apical region and posterior wall of the left ventricle. There was severe coronary sclerosis, with focal narrowing of all the major branches but no indication of recent thrombosis. The lungs were voluminous and somewhat emphysematous, and on section presented dark red moist congested surfaces, without evidence of bronchopneumonia. The liver parenchyma was strikingly soft and friable. The spleen was small and firm, and not remarkable, showing neither infarction nor fibrosis. The kidneys showed arteriosclerotic scarring, with slight reduction in size and evidence of congestion and parenchymatous degeneration. The stomach was dilated and contained about a liter of fluid material. The surface of the brain was congested, and serial section showed it to be peculiarly soft and congested throughout, although no significant focal lesions were discernible. From the gross findings alone, the cause of death was not clear, and the fatality was ascribed tentatively to hepatic damage, or possibly to cerebral injury.

Microscopic examination revealed a number of additional abnormalities that shed light on what had apparently happened in this case. Sections of the kidneys showed tremendously dilated, empty glomerular capillaries—a finding that prompted Dr. A. R. Rich, whom we consulted, astutely to suggest the possibility of fat embolism. The presence of fat globules within the glomerular tufts could not be demonstrated (although they may have been dissolved in the course of storage of the tissue blocks in alcohol). However, frozen sections of the lungs stained with sudan IV showed embolic occlusion by neutral fat of many of the alveolar capillaries and smaller pulmonary artery branches. The brain had not been preserved so that we were unable to do frozen sections in a search for fat emboli in the cerebral vessels. However, sections of the paraffin blocks showed congestion, focal demyelinization of the white matter, especially around blood vessels, and beginning reactive gliosis—findings resembling those described by Wertham and co-workers,[4] Groskloss,[5] Warren[6] and others in cases of

COMMENT

That fat embolism may develop following fractures, especially after surgical manipulation, is a commonplace observation.[7] The experience of the late war has also brought the full realization that fat embolism is a rather common and important cause of death after traumatic injuries in general, even without fracture of one or more bones.[8] Occasionally it may even be a consequence of severe burns. The explanation usually advanced in such cases is that fat particles mobilized from traumatized fatty bone marrow or other fat depots gain entry into the venous circulation, only to be trapped in the capillary bed of the lungs, and frequently of the brain, kidney and other organs as well. However, fat embolism is known to develop also in the absence of injury to fatty tissue, having been observed, for example, as a spontaneous phenomenon in cases of sickle cell anemia[9] and (rarely) in a variety of conditions characterized by lipemia.[7] Clearly, the explanation commonly invoked to account for fat embolism does not apply to such cases, and one must consider certain other possibilities. Thus, the source of the embolized fat globules may conceivably be the lipid envelope of erythrocytes in the blood, as Angrist[4] has cogently suggested in relation to fat embolism complicating sickle cell anemia. According to Leathes and Raper[10] the lipid content cerebral fat embolism. It should be mentioned also that the red cells appeared sickled in many places, but there were no changes in the spleen and other organs to indicate that sickle cell anemia had been present.

4. Wertham, F.; Mitchell, N., and Angrist, A.: The Brain in Sickle Cell Anemia, Arch. Neurol. & Psychiat. **47**: 752-767 (May) 1942.
5. Groskloss, H. H.: Fat Embolism, Yale J. Biol. & Med. **8**: 59-91 and 175-197, 1935; **8**: 297-316, 1936.
6. Warren, S.: Fat Embolism, Am. J. Path. **22**: 69-83 (Jan.) 1946.
7. Warthin, A. S.: Traumatic Lipaemia and Fatty Embolism, Internat. Clin. **4**: 171-227, 1913.
8. Robb-Smith, A. H. T.: Pulmonary Fat-Embolism, Lancet **1**: 135-141 (Feb. 1) 1941. Warren.[6]
9. Wade, L. J., and Stevenson, L. D.: Necrosis of the Bone Marrow with Fat Embolism in Sickle Cell Anemia, Am. J. Path. **17**: 47-54 (Jan.) 1941. Wertham, Mitchell and Angrist.[4]

of the red corpuscles is actually greater than that of the plasma, and is apparently labile, since its amount and composition change in the course of fat metabolism. Still another potential source of embolized fat is the emulsified fat in the blood plasma, and, indeed, the latter may well have played a role in the development of fat embolism in our case. In this connection, it is pertinent to cite the observations of Lehman and Moore[11] that fat emulsions can be broken up by ether and that dogs to whom ether is administered intravenously show significant fat embolism, the extent of fat embolism being enhanced by alimentary lipemia. Incidentally, in the case that we are reporting, the ether infusion that proved fatal was started about two hours after lunch, at which time alimentary lipemia might be expected to be at or near its peak.

The hazard of fat embolism is also of concern to anesthetists who occasionally employ ether intravenously, although the method does not appear to be in general favor. Fatalities have undoubtedly occurred after the intravenous use of ether as an anesthetic,[12] but we have been unable to find any reports in which the outcome was ascribed to fat embolism, although it is altogether possible that the latter was overlooked. Instances of fatal fat embolism, however, have been reported after anesthesia with chloroform[7] and cyclopropane,[13] which are, of course, also fat solvents.

In administering ether as a therapeutic agent, one must consider its effect on the liver also, in view of the accumulated evidence that ether may produce alterations in hepatic function, as well as anatomic evidences of injury to hepatic cells. Also, in view of the finding by Wirtschafter and Widmann[2] of gross hematuria and urinary casts in a number of patients so treated, one must take cognizance of possible alterations in renal function as well. Indeed, if the ether infusion method is to be employed for the treatment of peripheral vascular disease, it seems but a reasonable precaution to require that the status of hepatic and renal function be determined before and also at frequent intervals during the period of treatment and that further administration of ether be promptly discontinued if evidence of functional impairment be found.

SUMMARY

In a case in which the intravenous administration of ether was employed for the relief of peripheral vascular disease, a fatality ensued which autopsy showed to have resulted from pulmonary fat embolism. There were also microscopic changes in the brain indicative of cerebral fat embolism. Some of the implications of this experience are discussed. Attention is also directed to the necessity for safeguarding against irreparable hepatic and renal injury by ether administered intravenously.

10. Leathes, J. B., and Raper, H. S.: The Fats, ed. 2, London, Longmans, Green & Co., 1925, p. 149.
11. Lehman, E. P., and Moore, R. M.: Fat Embolism Including Experimental Production Without Trauma, Arch. Surg. **14**: 621-662 (March) 1927.
12. Betcher, A. M.: Personal communication to the authors.
13. Doud, E. A., and Roverstine, E. A.: Fatal Fat Embolism: A Case Report, Anesthesiology **7**: 291-295 (May) 1946.

Epidemics Traced to Cheese.—A summary of the data shows that during this time (since 1883) there has been a total of fifty-nine epidemics with 2,904 cases of disease and 117 deaths. There is every reason to believe that this represents only a fraction of the total. After the epidemics reported by Baker in Michigan during 1883-1884 no epidemics were recorded until 1893, after which there was a lapse of twenty-one years before another epidemic was reported. Thereafter, only an occasional epidemic due to cheese was reported until 1932, when the big epidemic occurred in Quebec, with 627 cases and 57 deaths. This epidemic seems to have made public health official conscious of the fact that cheese may be an important vehicle for the transmission of disease, and from that time on we find one or more epidemics reported each year except in 1933. From 1935 to 1945 forty epidemics were reported involving 1,741 cases and 47 deaths, which is over twice as many epidemics as the nineteen which were reported in the previous forty-two years. Such figures lead one to suspect strongly that during this time cheese had been overlooked as a source of disease. —Fabian, F. W.: Cheese and Its Relation to Disease, *Am. J. Pub. Health*, August 1947.

Council on Pharmacy and Chemistry

NEW AND NONOFFICIAL REMEDIES

The following additional articles have been accepted as conforming to the rules of the Council on Pharmacy and Chemistry of the American Medical Association for admission to New and Nonofficial Remedies. A copy of the rules on which the Council bases its action will be sent on application.

AUSTIN SMITH, M.D., *Secretary.*

OXIDIZED CELLULOSE.—Hemopak-Johnson & Johnson.—Absorbable cotton or gauze.—Cellulosic acid.—$(C_6H_8O_6)_n$.—M. W. n(176.12). Oxidized cellulose is prepared by the nitrogen dioxide oxidation of surgical gauze or cotton. Cellulosic acid is a polyanhydroglucuronic acid having a minimal carboxyl content of 16 per cent, a nitrogen content not in excess of 0.5 per cent derived from the nitrogen dioxide used in its preparation, and a formaldehyde content not in excess of 0.5 per cent derived from the formaldehyde used in its sterilization.

Actions and Uses.—Oxidized cellulose, a specially treated form of surgical gauze or cotton, exerts an unusual hemostatic effect and possesses the property of absorbability when buried in the tissues. Its hemostatic action is dependent on the formation of an artificial clot by cellulosic acid, which has a pronounced affinity for hemoglobin but does not enter per se into the physiologic mechanism of clotting. Absorbability depends on the size of the implant used, the adequacy of the blood supply to the area and the degree of chemical degradation of the material. Absorption of oxidized cellulose ordinarily occurs between the second and seventh day following implantation of the dry material, but complete absorption of large amounts of blood-soaked material may take six weeks or longer.

Oxidized cellulose is of value as an aid in surgery for the control of moderate bleeding under conditions where suturing or ligation is technically impractical or ineffective. Such situations include the control of capillary, venous or small arterial hemorrhage encountered in operations on the biliary tract, partial hepatectomy, resections or injuries of the pancreas, spleen or kidneys, bowel resections, amputations, resections of the breast, thyroid and prostate and in certain aspects of neurologic and otolaryngologic surgery. Oxidized gauze is employed as a sutured implant or temporary packing depending on the anatomic site or structures involved. Oxidized cotton is used primarily for neurologic surgery as unsutured packing, small portions of which may be left unremoved to control small areas of oozing from the dura or brain tissue. This material is likewise useful as temporary packing for control of secondary hemorrhage following adenoidectomy, tonsillectomy and other oral procedures and for control of alveolar bleeding following tooth extraction. Neither oxidized gauze nor cotton should be used for permanent packing or implantation in fractures, because it interferes with bony regeneration and may result in cyst formation.

The hemostatic action of oxidized cellulose is not enhanced by the addition of other hemostatic agents such as thrombin, which would be destroyed by the low p_H of the material, and it has been shown that the hemostatic action of either alone is greater than the combination. The hemostatic effect is greater when the dry material is applied, so that moistening with water or sodium chloride solution is not recommended. When properly used, oxidized cellulose may be closed in a clean wound without drainage, but this is hazardous whenever gross contamination is suspected or frank infection is present.

Neither oxidized gauze or cotton should be used as a surface dressing except for the immediate control of hemorrhage, as cellulosic acid inhibits epithelialization.

Dosage.—The amount of oxidized gauze or cotton used varies with the circumstances of the particualr case. As a general rule, only the minimal amount required to control hemorrhage should be used. For the control of hemorrhage from the prostatic bed, this may vary from one to four 2 by 14 inch (5.18 by 35.6 cm.) gauze packing strips, depending on the extent and vascularity of the area to be packed and the technic employed. This size of oxidized gauze is particularly designed for implantation by means of mattress sutures. Gauze packing strips ½ inch by 2½ yards (1.27 by 228.6 cm. are adapted for otolaryngologic or dental procedures; cotton pads 2 by 6 inches (5.08 by 15.24 cm.) are designed for neurologic, oral and/or dental surgical procedures.

In the event that it is desired to remove gauze or cotton from a hollow viscus or drainage site before dissolution is complete, removal can be facilitated by irrigation.

Tests and Standards.—

Oxidized cellulose in the form of gauze or cotton is slightly off-white in color, is acid to the taste and possesses a slight charred odor. It is soluble in dilute alkalie but insoluble in acids and water.

The solution obtained by vigorously shaking for one minute 200 mg. of oxidized cellulose in 10 cc. of 1 per cent aqueous sodium hydroxide solution, followed by the addition of 10 cc. of water, shows only a few fibers or foreign particles and only a slight haze. The presence of some swollen fibers may be tolerated if such fibers disappear when the solution has been standing for ten minutes. Addition of excess acid to the prepared solution causes a white, flocculent precipitate.

The moisture content of a 200 mg. sample of oxidized cellulose, when dried in vacuum over phosphorus pentoxide for twenty-four hours, does not exceed 15 per cent.

The residue on ignition of an accurately weighed specimen of oxidized cellulose does not exceed 0.15 per cent of the weight of the gauze or cotton.

Place 0.5 Gm. of oxidized cellulose, weighed to the nearest milligram, in a 125 cc. Erlenmeyer flask. Add 50 cc. of quarter-normal calcium acetate to the flask and swirl the contents until the sample is completely covered. Allow the mixture to stand for thirty minutes at room temperature, then titrate the solution with tenth-normal sodium hydroxide, using 5 drops of 5 per cent phenolphthalein T.S. as the indicator. Correct the titration by a blank run on 50 cc. of the calcium acetate solution. Each 1 cc. of tenth-normal sodium hydroxide is equivalent to 0.0045 Gm. of carboxyl group. The carboxyl content is not less than 16 per cent or more than 22 per cent, calculated on the dry basis.

Place a 1 Gm. sample of oxidized cellulose, weighed to the nearest milligram, in a 500 cc. Kjeldahl flask. Arrange a 125 cc. Erlenmeyer flask, containing 30 cc. of 4 per cent boric acid solution and 6 drops of mixed indicator (1 part of 0.1 per cent methyl red T.S. and 4 parts of 0.1 per cent bromcresol green T.S.), beneath the condenser of the distillation apparatus so that the tip of the condenser is well below the surface of the boric acid solution. Add to the Kjeldahl flask containing the sample 1 Gm. of Devarda's alloy (50 per cent copper, 45 per cent aluminum and 5 per cent zinc), 100 cc. of ammonia-free distilled water, a small lump of paraffin wax and 100 cc. of 5 per cent sodium hydroxide solution. Connect the Kjeldahl flask to the condenser by a suitable trap bulb. Heat the mixture in the flask until 45 to 50 cc. of distillate has collected in the receiver. Rinse the condenser and titrate the boric acid solution with tenth-normal sulfuric acid to a pale pink endpoint. Correct the titration by a blank run on the reagents in identical fashion. The nitrogen content shall not be more than 0.5 per cent, calculated on the dry basis.

To 1 Gm. of Oxidized cellulose in a 300 cc. Florence flask add 120 cc. of one times normal sulfuric acid and a few glass beads. Connect the reaction flask to an apparatus arranged for distillation with a dropping funnel filled with distilled water entering the flask. Transfer 10 cc. of a sodium bisulfite solution (13.7 Gm. sodium bisulfite or 12.5 Gm. sodium metabisulfite per liter in water) into a receiver so that the condenser outlet is submerged in the bisulfite solution. The contents of the reaction flask are heated to boiling, and during distillation distilled water is added to the reaction flask from the dropping funnel at such a rate that the volume of the contents of the reaction flask is not appreciably altered. Carry on the distillation for one hour, collecting 250 to 300 cc. of distillate. Cool the distillate, if warm, and allow it to stand for fifteen minutes to insure complete reaction of the bisulfite and formaldehyde. Add 1 cc. of starch T.S. and destroy the excess bisulfite by addition of tenth-normal iodine solution until a blue color is obtained. Discharge with a drop or two of tenth-normal sodium thiosulfate. Add 5 cc. of saturated sodium bicarbonate solution and titrate the liberated bisulfite with tenth-normal iodine. As the endpoint is approached, signaled by the very slow consumption of iodine, 0.5 cc. portions of half normal sodium carbonate are added, which discharge the blue color. The endpoint is reached when 1 cc. of the sodium carbonate solution does not discharge the blue color over a period of half an hour. Too great an excess of sodium carbonate is to be avoided since at high p_H the iodoform reaction may take place with an increased consumption of iodine. Each cc. of tenth-normal iodine solution is equivalent to 1.5 mg. of formaldehyde. The formaldehyde content should not exceed 4.5 per cent of the weight of oxidized cellulose calculated on the dry basis.

JOHNSON & JOHNSON, NEW BRUNSWICK, N. J.

Hemo-Pak Absorbable Gauze Packing Strip (4 ply) 2 by 14 inches (5.08 by 35.56 cc.) and ½ inch by 2½ yards (1.27 by 228.6 cc.) in sealed tubes.

Hemo-Pak Absorbable Cotton Pad: 2 by 6 inches (5.08 by 15.24 cc.) in sealed tubes.

U. S. trademark registration pending.

RIBOFLAVIN (See New and Nonofficial Remedies, 1947, p. 511).

The following additional dosage form has been accepted:

WALKER VITAMIN PRODUCTS, INC., MOUNT VERNON, N. Y.

Tablets Riboflavin: 10 mg.

SULFAMERAZINE (See New and Nonofficial Remedies, 1947, p. 125).

The following dosage form has been accepted:

ABBOTT LABORATORIES, NORTH CHICAGO, ILL.

Tablets Sulfamerazine: 0.5 Gm.

AMINOPHYLLINE (See New and Nonofficial Remedies, 1947, p. 305).

The following additional dosage form has been accepted:

CARROLL DUNHAM SMITH PHARMACAL COMPANY, NEW BRUNSWICK, N. J.

Tablets Aminophylline: 0.2 Gm. enteric coated with shellac.

THE JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

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SATURDAY, MARCH 20, 1948

EDITORIAL ANNOUNCEMENT

The absence of the compositors employed by the American Medical Association from their work continues. This issue of THE JOURNAL has been prepared largely by the use of Vari-Typer machines. Because of the difficulties of reorganization of the headquarters office necessitated by this situation, the editorial material in this issue of THE JOURNAL has been greatly condensed.

LEPROSY

World War II caused disruption of research on leprosy, and took essential personnel but did not stop progress. The most outstanding advancement in leprosy was made in clinical treatment. In 3 cases reported in a review by Dr. James A. Doull [1] successful surgical removal was apparently made of the primary lesion. In 2 cases evidence of dissemination of the disease had not appeared eleven years postoperatively. In the third case, that of a patient operated on in 1916, evidence of leprosy had not appeared on reexamination in 1944, twenty-eight years after excision of the original lesion. Use of diphtheria toxoid was considered to have failed to show beneficial results in treatment. This was equally true of transfusions of pooled blood plasma. Calcium gluconate was reported to give beneficial results when administered intravenously in cases of painful neuritis.

Preliminary reports of treatment with streptomycin were inconclusive. Many toxic manifestations were encountered, the most serious being tinnitus, impaired hearing and exfoliative dermatitis, and other reactions found to be associated with streptomycin therapy in other diseases.

Two groups of workers reported unsuccessful use of penicillin treatment. Dosages reached 100,000 units daily for periods of more than two weeks. Technics used were intramuscular injection every three hours, intravenous drip eight to ten hours daily and daily intramuscular injections of the drug in peanut oil and beeswax. The authors of these papers concluded that penicillin seemed to be useful in patients with secondary infections caused by streptococci or staphylococci. The dosages of penicillin were relatively small compared with extremely high penicillin dosages which have been found necessary for successful treatment in many cases of subacute bacterial endocarditis failing to show improvement on lesser dosage.

One author reporting on chaulmoogra oil stated that disagreement regarding therapeutic value of chaulmoogra is due essentially to lack of uniformity in selection of cases. Only the lepromatous type should be considered. He believed that the use of derivatives of chaulmoogra oil had achieved persistent clinical and bacteriologic negativation of lepromatous cases.

Dr. Doull reemphasizes the necessity for controlled case studies with the newer drugs. There is apparently some danger that plans for such control tests may be sabotaged on the one hand by a demand for treatment by every patient and on the other by the insidious belief that the response of treated patients furnishes a sufficient guide. The deceptive course of leprosy and the present continued uncertain position of chaulmoogra oil in therapy after years of administration is certainly convincing evidence of the necessity for adequately controlling experiments with newer drugs.

Sulfone drugs which have been used in leprosy are "promin," "diasone," "promizole" and "sulphetrone." The active principle of each of these seems to be diaminodiphenyl sulfone, the basic chemical from which they are derived. These drugs vary greatly in solubility and toxicity. The first report made by Faget and associates [2] stated that "promin" seemed to possess some chemotherapeutic property in leprosy, as evidenced by the apparent inhibition of the progress of the disease. This observation was subsequently confirmed by the same and other observers, who found that the improvement in leprosy under "promin" therapy is not accompanied by characteristic cellular changes. Cellular changes which do occur are atrophic in character, with extremely slow and gradual lessening of numbers of organisms in the lesions to the point of final disappearance. These changes do not differ materially from changes occurring during spontaneous remission without treatment of any sort. The important observation is apparently that "promin" eliminates bacillary infection in the blood vessels and blood stream, thereby preventing spread to new areas. Atrophy of focal lesions was found in locations with generous blood supply. Final conclusions were that a more highly bactericidal agent than "promin" appears necessary for chemical destruction of bacilli within tissue cells.

1. Doull, J. A.: The Journal: A Review of the Scientific Papers, Internat. J. Leprosy **15**: 444-465 (Oct.-Dec.) 1947.

2. Faget, G. H., and others: The Promin Treatment of Leprosy: A Progress Report, Pub. Health Rep. **58**: 1729-1741 (Nov. 26) 1943.

"Diasone" was reported on favorably in Trinidad, British West Indies, the National Leprosarium at Carville, La., and in Rosario, Argentina. Encouraging improvement occurred in patients treated, but bacilli did not completely disappear from lesions.

"Promizole" appeared to be well tolerated by patients with leprosy. Clinical improvement occasionally could be demonstrated more quickly with this drug than with "promin" or "diasone." There is disagreement with this on the basis that such a difference is not definitely established. This together with the distastefulness of the drug and its relative expense has led to its discontinuance in some clinics. "Sulphetrone" has been tried on only a few patients over a period of six months. Results are promising, and only mildly toxic symptoms have been observed.

Successful treatment of lepromatous ulcers was reported in 14 of 15 patients treated over periods varying from nineteen to seventy-five days with a 2 per cent alcoholic solution of tyrothricin. This solution is applied to ulcers in spray form. Crude streptomycin broth used locally has also been favorably reported.

Faget and Erickson [3] have stated that the sulfone drugs "promin," "diasone" and "promizole" produce objective clinical improvements in leprosy which are sustained and cannot be attributed to spontaneous remissions in the disease. These objective improvements, although slow in development, are progressive during the course of treatment. These authors [3] concluded that the sulfone drugs must be considered the optimal remedy for leprosy until faster acting remedies are discovered.

The long, unsettled and unsatisfying experience with chaulmoogra oil dictates that considerable caution be exercised in ascribing antileprotic qualities to any drug. However, recent developments with the sulfone derivatives indicates the probablity that a true chemotherapeutic agent may soon be discovered.

FAINTING AND FLYING

Romano and Engel [1] stated that encephalograms taken during actual loss of consciousness may be classified in three groups: the emotional type of fainting, the epileptic type and the syncopal or vasodepressor type. Rook similarly classified 500 cases of impairment of consciousness in pilots and air crew studied at the Central Medical Establishment, Royal Air Force. He considered the pathologic processes that led to the attack to result from three separate mechanisms: disturbances of the highest cortical levels; hypersensitivity of the nerve cells at the lower level leading either to explosive discharge or to pathologic inhibition, and alterations in the quantity or quality of the blood supply to the brain. The essence of loss of consciousness affirmed Rook, must be some change in the nerve cells themselves, whether brought about by mechanical, chemical or electrical agencies. Rarely in any case is only one of these pathologic processes at work. For example, emotion may be the trigger that unlooses an epileptic fit or causes an attack of syncope, as pointed out by Penfield and Erickson. The differentiation between an epileptic attack and cardiovascular syncope is not always easy. Epilepsy may be characterized by flaccidity rather than by convulsions, and convulsive movements are often seen in syncope. A reliable record of the patient is important. Psychiatric examination is helpful. Much controversial discussion ranges about the value of electroencephalograms. The exact value of encephalog raphic study has not been completely determined. A positive or negative electroencephalogram may be suggestive but no more. An electroencephalogram was done on 299 of the patients in Rook's series. In the neurogenic group nearly 50 per cent of the electroencephalograms pointed to an epileptic basis for the attack; in the other groups 15 per cent were positive. A change in the electroencephalogram when repeated occurred in 11 instances.

Of the 500 cases studied by Rook, 120 (24 per cent) were regarded as primarily neurogenic, 154 (31 per cent) as primarily due to some cardiovascular cause and 208 (42 per cent) as primarily emotional in origin. Seventeen cases could not be accurately classified. Pilots appear more likely to be affected than air crews. Fifty-three cases were definitely epileptic in origin, and 6 others were almost certainly epileptic. Hyperventilation of emotional origin in pilots and air crew was a frequent and a definite factor in the production of epilepsy. Fainting due to cardiovascular causes occurred because of cerebral anemia, cerebral congestion or some alteration in blood chemistry. Cerebral anemia was associated with heart disease, pain and hypotension; only rarely with hypertension. Cerebral anemia could be brought on by fatigue, excessive heat or cardiovascular inefficiency. Four instances concerned cerebral congestion and loss of consciousness associated with coughing.

The importance of emotion as a factor in the causation of loss of consciousness, particularly in wartime, is well known. Fear and anxiety and the various types of reaction to them are responsible for panic states and particularly for anxiety states. Inability to sustain the stress of flying and associated anxiety was present in 117 cases of this series. Simulation occurs in a few cases and is difficult to differentiate from hysteria.

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3. Faget, G. H., and Erickson, P. T.: Chemotherapy of Leprosy, J.A.M.A. **136**: 451-457 (Feb. 14) 1948.

1. Romano, J., and Engel, G. L.: Studies of Syncope; Differentiation Between Vasodepressor and Hysterical Fainting, Psychosom. Med. **7**: 3 (Jan.) 1945.

2. Rook, A. F.: Fainting and Flying, Quart. J. Med. **16**: 181 (July) 1947.

ELECTROPHORESIS AND PROTEIN FRACTIONATION

The methods of protein fractionation based on physical differences between the various fractions are peculiarly suitable for the identification and isolation of active protein principles. Even mild chemical treatment, such as precipitation with alcohol, appears at times to denature the active protein principle. In electrophoresis proteins are fractionated according to their rate of movement in an electrical field; this is dependent on the charge on the protein molecule and on its size and shape. In this procedure serum proteins are divided into the principal fractions: albumin; alpha, beta and gamma globulins, and fibrinogen.

The fractions obtained by electrophoresis, however, should not be considered to be chemically homogeneous without additional evidence, such as chemical analysis, crystallization, ultracentrifugal analysis and, perhaps most important, constant solubility. Insulin, for instance, appears to respond the same to electrophoresis, whether the preparation is crude or purified. In the study of pepsin and chymotrypsinogen, solubility has proved to be a more sensitive criterion of purity than electrophoresis. The electrophoretic fractionation of serum is dependent on the buffer which **is used; thus, the alpha-1-globulin in barbiturate buffer is included in the albumin fractions when phosphate buffer is employed.**

Characteristic electrophoretic patterns of the blood serum proteins have been found to be diagnostic of only a few diseases, such as nephrosis and some types of myalomatosis. Nephrosis is characterized by a profound reduction in serum albumin and gamma globulin while the alpha and beta globulins are increased. In most other cases, however, the electrophoretic picture appears to be characteristic not of the specific disease but of the host's reaction to infection or injury. The common denominator of almost every pathologic state thus examined is a relative or absolute decrease in serum albumin. Severe bodily injury, such as that due to burns, freezing or fractures of bones, results in decreased albumin and increased alpha globulin concentration. Infection results in two distinctive changes in the globulin fraction; in the febrile state there is usually an increase of alpha globulin to several times the normal concentration, though an exception to this increase is seen in malaria vivax due to Plasmodium. A later change is an increased concentration of gamma globulin, the fraction in which antibodies are found. In many infections fibrinogen is increased at an early stage along with alpha globulin. In tuberculosis the pattern changes with the progress of the disease: initially the **gamma globulin is elevated, then the alpha-2-globulin increases, and in far advanced cases all globulin fractions are augmented. Because of a decrease in albumin the total proteins remain essentially constant. The electrophoretic patterns of other pathologic states have also been reported, but, as with many chemical and physiologic measurements in disease, this information cannot in most cases be expected to yield a specific diagnosis of the disease. Additional information is needed for the more adequate interpretation of changes in plasma proteins.**

Current Comment

ELECTROLYTES AND WATER IN SHOCK

"Shock is a syndrome resulting from the depression of many functions, but in which reduction of the effective circulating volume and blood pressure are of basic importance and in which impairment of the circulation steadily progresses until it eventuates in a state of irreversible circulatory failure."[1] Extended discussion on the nature of the initiating factors in shock has appeared during the past quarter of a century with varying emphasis on their relative importance; however, the ultimate result is diminution of fluid within the blood vessels and the accompanying deleterious hemodynamic effects. Circulatory collapse is the outstanding clinical feature of shock from trauma or burns; in both circumstances it has not been possible to account satisfactorily for the loss of circulatory fluid by the accumulation of water in the tissues or the loss from the surface. A recent report[2] describes experiments designed to trace this "lost" water by following the shift in electrolytes from tissues subject to mechanical injury and to burns. With mice as the subjects, traumatic shock was produced in one hind leg and the opposite leg served as a control. There was a decided loss in potassium and a gain in sodium and water in the injured tissue. As sodium is the characteristic cation of extracellular fluid and potassium holds a like position in cell sap, the conclusion was reached that injury causes a loss of potassium from the tissue cells and a concomitant replacement with sodium and water, thus explaining the local edema. The passage of sodium from the extracellular fluid into the cell lowers the osmotic pressure of the extracellular fluid in the injured tissues and brings about the uptake of water which was observed in the control leg. Similar results were secured when shock was produced by immersing the leg in water at 75 C. The foregoing observations have been interpreted to indicate that as a result of trauma there exists an obvious loss of water as edema fluid or "weeping" at the site of injury and also a hidden loss brought about by swelling of all the uninjured cells of the body. Both circumstances contribute to the reduction of fluid in the circulatory system, thus setting the stage for the development of the clinical signs of shock. A secondary factor is the toxicity of the potassium liberated into the circulation from the injured tissue cells. Measures that are designed to reestablish normal extracellular fluid volume and concentration of sodium while removing the excess potassium would seem to constitute a rational first approach to effective therapy.

1. Wiggers, C. J.: Physiol. Rev. **22**: 74, 1942.

2. Fox, C. L., Jr., and Baer, H.: Am. J. Physiol. **151**: 155 (Nov.) 1947.

Official Notes

MEETING OF THE BOARD OF TRUSTEES

A CONDENSED REPORT

Chicago, Feb. 19 and 20, 1948

The meeting of the Board of Trustees in Chicago on February 19 and 20 was fully attended, with the exception of Dr. John H. Fitzgibbon.

Fourth International Congresses on Tropical Medicine and Malaria

The Board voted to join the Fourth International Congresses on Tropical Medicine and Malaria as a sustaining member.

Grass Roots Conference

It was decided that the Grass Roots Conference shall be a part of the Annual Session in June and that it shall be held on Sunday afternoon as heretofore. Dr. A. M. Mitchell was selected as chairman of the conference.

Appointment of Representatives

Representatives were appointed to the Committee on Maternal and Child Health and Crippled Children's Services, to the American Academy of Political and Social Science, to the annual meeting of the British Medical Association, to the Midwest Physical Education Association, to the National Conference on Higher Education, to the ninth International Congress on Industrial Health to be held in London September 12-17 and to the Conference on Human Rights and Freedom of Information to be held in Washington, D. C., on March 4.

Dr. Fishbein was authorized to serve as chairman of the council of the International Medical Press, which proposes to hold a conference of medical editors of the world within the next few years.

Drs. E. L. Henderson and R. L. Sensenich were appointed as delegates to the meeting of the World Medical Association and Drs. E. E. Irons and Morris Fishbein as alternates.

Consultant for Council on National Emergency Medical Service

The appointment of Dr. Hugh Morgan as a consultant to the Council on National Emergency Medical Service on matters pertaining to the Army was approved.

Committee Appointments

The following committees were appointed: Committee on Hospital Competition with Private Practice; Committee to Work with the American National Red Cross on its blood bank program, and a Committee to work out a plan for the selection of the recipient of the General Practitioner's medal.

International Congress of Leprosy

Mr. Ralph Creer, secretary of the Committee on Medical Motion Pictures of the A.M.A., was authorized to accept an invitation from the Leonard Wood Memorial Institute (the American Leprosy Foundation) to attend the International Congress of Leprosy, which is to be held in Havana, Cuba, April 3-11.

Appointment of Consultants for Council on Industrial Health

Authorization was given to the Council on Industrial health for the appointment of a group of consultants having special attainments in the field of workmen's compensation to assist in the proper evaluation of medical and administrative policy and relations.

Exhibit on Medical Aspects of Atomic Energy

Approval was given for an exhibit by the Council on Physical Medicine at the Chicago Session on the medical aspects of atomic energy.

Session on Physical Medicine of Section on Miscellaneous Topics

Authorization was given for a Session on Physical Medicine in the Section on Miscellaneous Topics at the June Session of the Association

Conference on Nomenclature

Authorization was given for the calling of a conference on nomenclature on Wednesday afternoon, June 23, in the headquarters of the Association.

Survey of Medical Education

The following proposals of the Council on Medical Education and Hospitals were approved:

1. That the survey of medical education should be initiated at the earliest possible date.
2. That a committee consisting of Drs. Arthur C. Bachmeyer, Joseph C. Hinsey, Victor Johnson, and H. G. Weiskotten, and the secretaries of the Council on Medical Education and Hospitals and the Association of American Medical Colleges ex officio, supervise the conduct of the survey and prepare and publish a report.
3. That the employment of a full time director and such other personnel as may be needed to conduct the survey be authorized.
4. That the headquarters of the survey be maintained in the office of the Council on Medical Education and Hospitals.
5. That this survey be designated a Survey of Medical Education, sponsored by the Council on Medical Education and Hospitals of the American Medical Association and the Association of American Medical College, and be conducted by the committee whose membership is listed in paragraph 2.

The Board suggested that the name of an outstanding educator be added to the names of the committee members mentioned in paragraph 2, and the suggestion was adopted by the joint committee.

Appointments to Editorial Boards, Councils and Committees

Appointments were made to various editorial boards, councils and committees to fill vacancies caused by the expiration of terms of service.

Dr. Stanley J. Seeger Named Emeritus Chairman of Council on Industrial Health

The Board voted that Dr. Stanley J. Seeger, who recently resigned from the Council on Industrial Health, be named emeritus chairman of that Council.

Fund-Raising Campaign of American Cancer Society

The Board authorized the publication of an editorial in support of the campaign of the American Cancer Society for funds.

Successor to Dr. Lloyd Noland on Judicial Council

The Board noted with regret the resignation of Dr. Lloyd Noland from the Judicial Council and approved the appointment by the President of Dr. Homer Pearson to fill the vacancy on the council until the next meeting of the House of Delegates.

Nurse Anesthetists

The attention of the Board was called to articles being published in the lay press regarding nurse anesthetists, and it was voted to condemn publicity that is not based on a scientific understanding and that does not accurately reflect the prevailing situation.

Handbook of American Medical Association

The Board voted to publish an announcement in THE JOURNAL that copies of the Handbook of the American Medical Association are available in the headquarters office.

American Academy of General Practice

A conference was held with officers of the American Academy of General Practice, and the Board appointed a liaison committee to that organization, consisting of Dr. Harvey B. Stone from the Council on Medical Education and Hospitals, Dr. E. J. McCormick from the Council on Medical Service and Dr. Wingate M. Johnson from the Board of Trustees.

Proposed Amendment to Internal Revenue Code

The Board authorized its representatives to a meeting of the New York Bar Association to record the vote of the Board in support in principle of the proposal that the Internal Revenue Code be amended to permit physicians doing business as a partnership to deduct the cost of a pension program for themselves and to accord physicians and others doing business as proprietors the same privilege, with the proviso that there should be a reasonable maximum.

Voluntary Support of Medical Education

The need and desirability of developing and organizing a continuing program on a national scale for the promotion of voluntary support of medical education was recognized and the Board authorized that a campaign be conducted.

Funds for Medical Education

In considering bills S. 145 and H. R. 3925, the Board expressed disapproval of the use of federal funds for medical education in any manner by which the government would enter into control.

Registration and Approval of Hospitals for Internship and Residencies

At a meeting on Saturday of a special committee appointed by the Board of Trustees and representatives of the American College of Surgeons, the Council on Medical Education and Hospitals, the American Board of Surgery, the American Board of Orthopedic Surgery and the Advisory Board for Medical Specialties, it was decided to appoint a committee of seven; two members to represent the American Medical Association; two, the American College of Surgeons; two, the specialty boards in surgery, and the secretary of the Advisory Board for Medical Specialties to study the whole matter of the registration of hospitals and their certification for internships and residencies and to work out a mechanism that will avoid duplication. The conference group selected Drs. W. M. Firor of Baltimore and Guy A. Caldwell of New Orleans to represent the specialty boards in surgery; the special committee of the Board selected Drs. Harvey B. Stone and Donald G. Anderson to represent the American Medical Association, and Drs. F. A. Coller of Ann Arbor, Mich., and Dallas Phemister of Chicago have been appointed by the board of regents of the American College of Surgeons to represent that organization. The secretary of the Advisory Board for Medical Specialties is Dr. B. R. Kirklin.

Correction of Inaccuracies in Pronouncement of Dr. Parran Re Shortage of Physicians

The Board voted to request correction of the inaccuracies in the pronouncement of Dr. Thomas Parran, Surgeon General of the United States Public Health Service, with respect to the critical shortage of physicians in the United States which he anticipates will develop by 1960.

Medical Motion Picture Film for British Medical Association

The Board voted to send, with the compliments of the Association, a copy of its film "Medical Motion Picture: Its Development and Present Application" to the Library of the British Medical Association.

Dr. Fishbein to Cooperate in Preparation of Series of Medical Motion Pictures

The Board authorized Dr. Fishbein to continue negotiations with film producers with a view to extending medical education to the public through the use of scientific medical pictures.

Miscellaneous

Many other subjects were considered. Some of them will no doubt come up again for action.

WASHINGTON LETTER

(From a Special Correspondent)

Feb. 18, 1948

Shortage of Physicians in Armed Forces on Increase

Rear Admiral Joel T. Boone, executive secretary, Armed Services Committee on Medical and Hospital Services, following a tour of Army, Navy and Air Force hospitals reported that the shortage of physicians in the armed services is increasing and may endanger the health of American fighting men. The committee is studying possible administrative changes in the service medical departments as a result of unification. Admiral Boone explained that about half of the military physicians now on duty will leave service by July 1, 1949, when the Navy V-12 and the Army specialized training programs end. Under these programs young men were taken into the services and trained as physicians. The admiral estimated that the Navy's staff of physicians would drop frmm 2,900 to 1,482 while the Army would lose about 3,000.

Veterans' Budget Seeks More Medical Personnel

The proposed 1949 budget of the Veterans Administration is reported to provide for a slight increase in medical personnel but a decrease in administrative workers. Veterans Administrator Gray is reported to have refused the request of a House Veterans Committee to delay the current dismissal of 8,500 employees of the agency. The committee had asked for delay in their release until the effect of such dismissal on service to veterans could be ascertained. The agency in a statement explained that the cuts in staff were ordered because present funds "are not sufficient to maintain services and employment at the present level."

Committee Approves Funds for Research Center

The House Appropriations Committee approved immediate provision of $5,000,000 and authorization to spend $40,000,000 to build an eight hundred bed hospital and research center at Bethesda, Md., to house research on mental disorders, heart disease and cancer. The committee reported out the Labor-Federal Security supply bill for 1949 and added $8,000,000 to the original request for funds for the center. An escalator clause was inserted to assure that work starts promptly and that the center is completed as soon as possible. The Federal Security Agency is permitted to contract in excess of $40,000,000 if rising costs of building make this necessary.

GOVERNMENT SERVICES

ARMY

NEW APPROACH TO CONTROL OF VENEREAL DISEASE

Following studies made in 1946, the Army developed a new approach to the control of venereal disease. A phenomenal decrease in the number of cases in American soldiers occurred during 1947. The decrease for the Army as a whole amounted to 40 per cent, and among the soldiers stationed in the United States it amounted to more than 50 per cent.

In considering methods for the control of venereal disease the general staff established the Army Venereal Disease Control Council. Local councils were established at all military installations. There emerged a program, now employed, based on moral, spiritual, psychologic and objective factors. This broadened approach has supplanted previous concepts. Today stress on the moral reasons for good conduct is imparted to the troops through group and individual instruction. Planned entertainment helps to maintain the wholesome interest of the soldier and keeps him off the street when he is off duty. A further aid was the recall of all training films used during the war for venereal disease control and the production of new films reflecting the present program. The first in the new series of motion pictures is entitled "The Miracle of Living"; it dramatizes the rewards of good conduct as well as the effects of venereal diseases on the person's future.

ARMY NURSE CORPS RESERVE

The Surgeon General has summoned fifty Army Nurse Corps leaders to Washington for a two day conference to map out a program to enroll 29,000 Army Nurse Corps officers during 1948, about 25,000 of whom are to accept commissions on an inactive status, continuing in their civilian posts except in time of national emergency. Attending the conference are chief nurses of the six Army areas in the United States and of Army general hospitals and the directors of nursing services in the Far East Command, in Europe and the Antilles.

Under the provisions of an act of Congress of 1947, the Army Nurse Corps became a permanent branch of the military establishment. The law provided for the formation of a reserve corps through which all future assignments of nurses to extended active duty will be made. About two thousand such assignments will be available during 1948.

MEDICAL MEETING IN KOREA

About seventy-five officers attended the medical meeting February 18 at the 382d Station Hospital in Korea The forenoon was given over to ward rounds and departmental conferences. In the afternoon Major Robert M. Hardaway, chief, surgical service, 34th General Hospital, read a paper on regional ileitis; treatment was discussed by Lieut. Wilbur A. Thomas of the 34th General Hospital. Lieut. Col. Warner F. Bowers, surgical consultant (GHQ, FEC) discussed abdominal trauma and the cases observed on the surgical ward rounds. Lieut. Ross A. Miller, chief, surgical service, 382d Station Hospital, read a paper on acute intestinal obstruction, which was discussed by Lieut. Cecil A. White of the 382d Station Hospital and Lieutenant Col. Bowers. Capt. Myrtle N. Nereson, chief, principal nurse, 382d Station Hospital, discussed "The Nursing Care of Colostomies" The scientific session was under the direction of Lieut. Col. Watson E. Neiman, commanding officer, 382d Station Hospital, and the business meeting was presided over by Col. Charles P. Ward, surgeon, 24th Corps. A buffet dinner and social hour were held at the Officer's Club in the evening.

NAVY

NEW REGULAR OFFICERS

The following five lieutenants (jg), all graduates of the Navy's V-12 program, have been transferred to the Regular Navy Medical Corps: Richard B. Connor, Columbia, S.C.; Kevin A. Doyle, Glenbrook, Conn.; Avery L. Cotton, Houston, Texas; Charles L. Lear, Montebello, Calif.; and Fred A. Valusek, Newburgh, N.Y.

The following physicians from civil life have recently been commissioned lieutenants in the Regular Navy Medical Corps: George E. Gardner, Philadelphia, and James M. Tuholski, Memphis, Tenn.

RESERVE OFFICERS NOMINATED FOR DUTY

The following lieutenants (jg) of the naval medical reserve, having completed the basic refresher course at the Naval Medical School at Bethesda, Md., have been nominated for duty; James E. Hull, Columbia City, Ind.; Dwight H. Smith, Cherry Point, N.C.; DeWitt T. Brock, Camp Lejeune, N.C.; James R. Clarkin, Bronx, N.Y.; John R. Lindsay, Wilmington, Del.; Charles E. Boonstra, Lafayette, Ind.; Richard K. Williams, Richmond, Va.; Archie G. Britt, La-Crosse, Wis.; John E. LeDonne, Revere, Mass.; Howard H. Lyons, Linwood, Mass.; Donald H. McCowan, West Chester, Penn., and Grover C. Nabors, Goldville, S.C.

GRADUATE TRAINING

The following medical officers have been approved for graduate training: Comdr. Edward G. Hurlburt, residency in dermatology and syphilology at a Navy Hospital.

Comdr. Joseph A. Forte, course in internal medicine at University of Pennsylvania Graduate School of Medicine, beginning October 1948.

Lieut. Comdr. Ralph D. Ross, additional year's training in internal medicine at the Naval Hospital, San Diego, Calif.

Lieut. (jg) Robert W. Williams Jr., residency in in internal medicine at a Naval hospital.

Lieut. Dale B. Watkins, additional year's training in internal medicine at the Naval Hospital, San San Diego, Calif.

Lieut. (jg) Orville M. Graves Jr., residency in ophthalmology at the Naval Hospital, San Diego, Calif., transfer to U. S. Navy.

Lieut. (jg) John R. Huston, residency in pathology at a Naval Hospital.

Comdr. Lewis E. Hedgecock, course in preventive medicine and venereal disease control at Johns Hopkins University School of Hygiene and Public Health, Baltimore.

Comdr. William F. Lyons, course in preventive medicine at Harvard University, Boston.

Comdr. Theodore E. Hoffman, residency in surgery at the Naval Hospital, Great Lakes, Ill.

Comdr. Richard Lawrence Jr., residency in internal medicine, U.S. Naval Hospital, San Diego, Calif.

Lieut. (jg) Preston R. Bandy, residency in anesthesiology, Naval Hospital, Bethesda, Md.

Comdr. Ronald N. Shelley, course in thoracic surgery and endoscopy at George Washington University School of Medicine, Washington, D.C.

Lieut. (jg) James I. Thorn, training in aviation medicine, School of Aviation Medicine and Research Naval Air Station, Pensacola, Fla.

Capt. Julian Love, Comdr. Bishop L. Malpass and Comdr. Ross W. Weisiger have completed a course of instruction in internal medicine at Cornell University Medical College, New York.

MISCELLANEOUS

ATOMIC COMMISSION TO SUPPORT CANCER RESEARCH

The Atomic Energy Commission is expanding its assistance to the nationwide work on cancer research by a program which involves radioactive materials, new facilities and financial aid. The program was designed to explore the possible benefits of atomic energy to those with cancer, to assist existing projects and to avoid duplication of work carried on by other governmental agencies, the American Cancer Society and privately endowed foundations and medical research centers. The main points of the commission's assistance are: (1) provision of radioisotopes for cancer research and treatment by qualified United States medical and research workers; (2) support of selected cancer research projects carried on by hospitals and universities; (3) establishment of research facilities, including limited hospital space at four laboratories of the commission, and (4) support of cancer research carried on by the Committee on Atomic Casualties of the National Research Council.

Effective April 1, 1948 all charges except those for handling and transportation will be removed from radioactive iodine (I 131) phosphorus (P 32) and sodium Na(24) to be used in the study and treatment of cancer. Other available useful radioisotopes will be added to the list, as it is determined that they can be supplied on the new basis. The commission warns that radioisotopes have not been found generally useful in cancer treatment as developed at the present time.

These radioisotopes under the new procedure will be obtained as heretofore from the Isotopes Branch, Atomic Energy Commission, Oak Ridge, Tenn.

I 131 has a relatively short half life. Half of its radioactivity is lost after eight days, half of the remainder by the end of the next eight days and so forth. The physician or investigator using the material must make allowance for loss of radioactivity as a result of time lost in shipment. If shipment requires five days, for example, a physician must order about 10 millicuries of I^{131} for every 6 millicuries of material he wishes to administer. The purchase price of I^{131} at Oak Ridge, Tenn., has been $1.70 per millicurie, the unit in which radioactivity is measured. Individual patients may receive a single application of only a few millicuries or a course of treatment extending over a period of weeks, so that the cost of material, apart from handling and shipping, may range from $20 to $200 or more. The price of Na^{24} has been $12 per irradiated unit, which contains approximately 20 millicuries. This material has a relatively short half life, and, if an investigation is to extend for a considerable period of time, new lots of material must be procured at frequent intervals. Often an investigator will place an order for one or two units per week, extending over a period of six months or more, so that the saving in cost of material may amount to several hundred dollars.

In announcing increased support for selected cancer research projects related to atomic energy and carried on by independent institutions in various parts of the nation, the commission pointed out that projects which it supports are already under way at the Memorial Hospital for Treatment of Cancer and Allied Diseases, New York; Harvard University; the University of Rochester, and the University of California. At other institutions projects are being selected for support from the special fund for research on cancer now set aside by the commission.

Cancer research facilities will be established at Oak Ridge Hospital, Oak Ridge, Tenn.; Brookhaven National Laboratory, Long Island, N. Y.; Argonne National Laboratory, Chicago, and Los Alamos Laboratory, Los Alamos, N. Mex. Medical schools, clinics, hospitals and other research institutions in each region will be able to make use of the unique equipment in these installations.

The commission emphasized that its part is to provide the facilities to investigators or patients: the research will be carried on by the investigators, not by the commission; also, the hospital beds and research facilities will not be available for the treatment of cancer patients in general. With the limited number of beds, it is necessary that they be used for special studies which may benefit many who suffer with cancer through adding to basic knowledge, rather than solely for treatment of the few who can be accommodated.

FOREIGN SCHOLARSHIPS AVAILABLE SOON

The Fulbright Act authorizes executive agreements with foreign governments under which they may pay in part for sales of American surplus property overseas with scholarships and other educational enterprises in their own countries for American students. The State Department announces that in addition to agreements with China and Burma draft agreements are under consideration by the Philippines, Italy, New Zealand, Greece, Egypt and Belgium. Twenty-two nations are now eligible and are expected to participate in the plan, with an indication that more than $140,000,000 will be devoted to the program within the next twenty years.

Under agreements already completed China and Burma have placed at the disposal of the United States sums which will be used for financing studies, research, instruction and other educational activities for American students in schools in Burma and China. These sums include also the cost of transportation to and from the United States, tuition, maintenance and incidental expenses; they will permit Burmese and Chinese students to study in United States schools located outside this country as well as paying the cost of transportation of foreign students to and from the United States. Plans for making grants available to American scholars have not been completed, but public announcement will be made of the date when application can be received, which is expected to be early in 1948. Additional information can be obtained by writing the Division of International Exchange of Persons, Department of State, Washington 25, D. C.

Medical News

(Physicians will confer a favor by sending for this department items of news of general interest: such as relate to society activities, new hospitals, education and public health. Programs should be received at least two weeks before the date of meeting.)

ARKANSAS

State Medical Meeting.—The Arkansas Medical Society will hold its annual meeting in Little Rock April 15-17 under the presidency of Dr. Lorenzo T. Evans, Batesville. Out of state speakers include:

Irvin E. Hendryson, Denver, Early Diagnosis of Poliomyelitis. Harry E. Bacon, Philadelphia, Cancer of Rectum, and Pelvic Colon.

Paul A. Davis, Akron, Ohio, General Practice of Medicine as related to the American Academy of General Practice. Hedwig S. Kuhn, Hammond, Ind., Industrial Ophthalmology. Ralph L. Ferguson, Vermillion, S.D., The Lymph Node as an Aid in Diagnosis. Carl A. Nau, Galveston, Texas subject to be announced. Richard Cattell, Boston, subject to be announced.

The Past-President's Breakfast will be held at the Hotel Marion April 17 at 7:30 a.m.

CALIFORNIA

Chronic Disease Survey.—At the direction of the 1947 state legislature, the state department of public health has formulated a plan for an extensive investigation of the "problems involved in the reduction of deaths and disability from cancer and other chronic diseases." The outline of the plan was approved by the state board of public health in November, and an advisory committee which was appointed at that time has held its initial meeting. Recommendations and estimated program costs will be placed before the legislature in 1949.

Open Nursery at Stanford Hospital.—A $20,000, fifty-eight crib nursery designed to prevent dangers of diarrhea and respiratory and cutaneous infections, was opened for inspection February 19 at Stanford University Hospital, San Francisco. Each crib is self contained, having its own equipment to prevent cross infection. Funds were provided by the late Mrs. Richard H. Shainwald and her brother, Walter D. Heller, San Francisco, in memory of their parents, Dr. and Mrs. Moses Heller.

FLORIDA

Annual Meeting of Board of Health.--The state board of health, at its annual meeting on February 10, recommended the expansion of four definite activities: abatement of stream pollution with special reference to Florida's beaches and streams; expansion of the Food Handlers' School; intensification of the school health program, and encouragement of counties to provide better quarters for their health units. The board reelected Dr. Herbert L. Bryans, Pensacola, as president. Dr. Wilson T. Sowder, state health officer, is executive secretary.

ILLINOIS

New Wing at County Hospital.--The Memorial Hospital of Du Page County, Elmhurst, recently opened a new $750,000 wing which adds one hundred beds to the one hundred and twenty-five beds in service, provides new surgical suites, a pediatric unit, auditorium and medical record library and will permit enlargement of the x-ray department, emergency section and delivery rooms. The Du Page County Medical Society, which henceforth will hold its meetings at the hospital, heard Dr. Willis J. Potts, Chicago, speak on "Recent Advances in Children's Surgery" at the opening of the new auditorium on February 18.

Chicago

Personal.--In January Dr. Leon Unger lectured on bronchial asthma before the Sociedad Mexicana de Alergistas in San Luis Potosi, Mexico, and later before the staff of the Children's Hospital, Mexico, D.F.

The Bacon Lectures.--Dr. Nicholson J. Eastman, professor of obstetrics at Johns Hopkins University School of Medicine, Baltimore, will deliver the annual Charles Sumner Bacon lecture at 1 p.m. April 14 at the University of Illinois College of Medicine on "Pelvic Mensuration; a Study in the Perpetuation of Error." The Bacon series was inaugurated in 1928 in honor of the late professor emeritus of obstetrics and gynecology. At that time members of the faculty and friends of Dr. Bacon contributed $5,000 to found the lectureship.

KANSAS

Dr. Murphy Appointed Dean.—Dr. Franklin D. Murphy, Kansas City, has been appointed dean of the University of Kansas School of Medicine effective July 1 to succeed Dr. Harry R. Wahl, dean since 1924. Besides serving as dean, Dr. Murphy will be an associate professor of internal medicine. He is the son of the late Dr. Franklin E. Murphy, a founder of the medical school and member of the faculty. Dr. Murphy obtained his medical degree at the University of Pennsylvania School of Medicine, Philadelphia, 1941; from 1944 to 1946 he was a captain in the army medical corps and worked with a research unit at Memphis, Tenn. Dean Wahl, who asked to be relieved of his duties as dean a year ago, will continue to teach at the medical school as head of the department of pathology.

LOUISIANA

Public Relations Program.—The Council on Medical Service and Public Relations of the Louisiana state Medical Society has developed a public relations program which provides for radio programs on health. A Speakers Bureau is to be established and lay persons and members of the profession will appear before all interested groups to talk on health, economics of medicine, voluntary health insurance and other subjects. An educational health column is to be released weekly for newspapers throughout Louisiana. A News Bureau will be established to disseminate information to the public relative to scientific advancements by members of the medical profession and to advise the public what the medical profession is doing in their behalf. The Louisiana Physjcians Service, offering surgical and obstetric care, is sponsored by the Louisiana State Medical Society. It is proposed that the society assist in the establishment of health councils in every parish throughout the state. Other phases of the program include a closer relationship with other health agencies, societies and civic clubs and a campaign to enhance patient-physician relations. In general, the program will provide a medium to maintain adequate medical care at a cost which the patients can afford and at the same time to keep medicine a private enterprise.

MARYLAND

McCollum-Pratt Fund.—Johns Hopkins University, Baltimore, has received a $500,000 endowment, the McCollum-Pratt Fund, to be used for study of the function of copper, boron, cobalt, manganese and other minerals in living organisms. The principal and interest will be expended over a ten year period. The fund was named in honor of Elmer V. McCollum, LL.D., an authority on nutrition, and John L. Pratt, Fredericksburg, Va., university trustee and donor.

MICHIGAN

Ophthalmologic Clinics.—Dr. Albert D. Ruedemann, professor of ophthalmology, Wayne University College of Medicine, Detroit, will give clinics on beta irradiation in ophthalmology at the City of Detroit Receiving Hospital every other Wednesday from 10 a.m. to noon until June, beginning March 10. All ethical specialists are invited to attend.

MINNESOTA

Society of Anesthesiologists.—At a meeting in Minneapolis Nov. 15, 1947, a group of members of the American Society of Anesthesiologists formed the Minnesota Society of Anesthesiologists as an affiliate of the national organization. Dr. Ralph T. Knight, Minneapolis, was elected president and Dr. Frank Cole, Duluth, secretary-treasurer.

The Judd Lecture in Surgery.—The fifteenth E. Starr Judd Lecture will be given by Dr. Alfred W. Adson, professor of neuro-surgery at the Mayo Foundation, Rochester, April 29 at 8:15 p. m. in the Auditorium of the Museum of Natural History. Dr. Adson's subject is "The Evolution of Neurosurgery." The late E. Starr Judd, an alumnus of the University of Minnesota Medical School, established this annual lectureship in surgery a few years before his death.

Cancer Detection Center Opens.—A cancer detection center operating on a research basis opened in February at the University of Minnesota Hospital, Minneapolis. The effectiveness of examining apparently well persons in order to find early cancer will be determined. Persons who need treatment will be referred to their physicians. The center is financed by the Minnesota Division of the American Cancer Society, the U. S. Public Health Service and the University of Minnesota. Dr. David State of the hospital staff will serve as acting director. The center is to be open Tuesday and Thursday afternoons from 3 to 5 o'clock. Examinations will be by appointment only

Dr. Colvin Honored.—The surgical staff of the Ancker Hospital, St. Pall, honored Dr. Alexander R. Colvin at a dinner in the Minnesota Club January 19. Dr. Colvin has practiced in St. Paul since 1903 except for his service in the army medical corps during World War I. He has for the past thirty years been head of the surgical service of the hospital.

X-Ray Surveys at Colleges and State Institutions.—The Minnesota pepartment of Health launched its x-ray survey program in January. The goal is an annual roentgenologic examination of the chest of every Minnesota college student and all persons in state institutions. Colleges are assisting in financing the program. The state program combined with a community mass x-ray survey are expected by 1950 to bring to every person in the state an opportunity for roentgenologic examination.

MISSISSIPPI

Scholarship Loan Applications. -- The state medical education board has announced that all students interested in applying for medical education scholarship loans to become effective in autumn of 1948 should contact the Jackson office of the board, Room 37, North Street Building at once for information and application forms. Applications received during the spring months will be considered by the board on and after June 1. Over a hundred students have already requested applications for medical education loans to become effective in September.

NEW MEXICO

Clinical Society Lectures.—The New Mexico Clinical Society has arranged a schedule of lectures for the next few months to be held in the Museum of Anthropology, Santa Fe, with the following speakers:

April 16, Chester M. Jones, gastroenterologist, Harvard Medical School, Boston.
April 30, Francis Rackemann, allergist, Harvard.
May 3, Hamilton Montgomery, dermatologist, Mayo Clinic, Rochester, Minn.
May 14, Walter C. Alvarez, gastroenterologist, Mayo Clinic
June--Peter Heinbecker, surgeon, Washington University School of Medicine, St Louis.
July--Louis S Goodman, pharmacologist, University of Utah, Salt Lake City.
August--Oscar O. T Clagett, chest surgeon, Mayo Clinic, Rochester Minn. C. Allen Good, radiologist, Mayo Clinic, Rochester, Minn.

OHIO

Memorial Library.—The library at Peoples Hospital, Akron, consisting of about seven hundred selected volumes, including many of the current periodicals, has been named in honor of Dr. Jay D. Smith. He was interested in medical education and gave freely of his time and thought to Peoples Hospital while a member of the surgical staff from 1914 until his death, Nov. 17, 1947.

Appointed Head of Department of Urology.—Dr. Charles C. Higgins, Cleveland, has been named head of the department of urology at the Cleveland Clinic to succeed Dr. William E. Lower, one of the four founders of the Cleveland Clinic, who is retiring from active practice. Dr. Higgins graduated in medicine from Washington University School of Medicine, St. Louis, in 1923. He is president-elect of the American Urological Association, president of the Clinical Society of Genito-Urinary Surgeons and a member of the American Board of Urology.

PENNSYLVANIA

State Society to Publish History.—The history of the Medical Society of the State of Pennsylvania is being prepared in book form for publication in connection with the centennial celebration of the organization in October. Dr. Howard K. Petry, Harrisburg, former president of the society, is in charge of research, writing and production of the history. Authentic stories of unusual interest relating to physicians of bygone years will be welcomed by Dr. Petry for consideration. The headquarters of the society is at 230 State Street, Harrisburg.

Philadelphia

Faculty Appointments.—Hahnemann Medical College has announced the appointment of the following: Dr. John E. Gregory, Philadelphia, professor of pathology and head of the division of pathology; Amedeo Bondi, Jr., Ph.D., professor of bacteriology and head of the department, and Dr. Emerson A. Read, Quincy, Mass., assistant professor of physiology. Four newly appointed full time instructors in the clinical departments are Dr. Alexander W. Ulin, Cincinnati department of surgery; Drs. Otto H. Janton, Detroit, and Albert M. Lupton, Lewes, Del., department of medicine, and Dr. Joseph N. Seitchik, Philadelphia, department of obstetrics

County Postgradute Institute.—The twelfth Annual Postgraduate Institute of the Philadelphia County Medical Society will be held at the Bellevue Stratford Hotel, April 20-23. Topics to be discussed include: problems in obstetrics and gynecology, newer drugs and procedures, surgery of the ambulatory patient, fractures, the painful breast, neuropsychiatric disorders, problems of the aged, the acute abdomen, gastrointestinal disorders and otolaryngolical problems. At two evening sessions cancer and pediatrics will be discussed. For information address Dr. Gilson Colby Engel, Director, 301 South Twenty-first Street, Philadelphia 3.

TEXAS

Society Election.—The Texas Radiological Society on January 17 elected Dr. Leslie M. Garrett, Corpus Christi, president; Dr. John J. Faust, Tyler, president-elect; Dr. Roscoe P. O'Bannon, Fort Worth, secretary-treasurer. The next annual meeting will be held in Fort Worth January 7-8, 1949.

Rehabilitation Clinic Dedicated—At a conference on physical medicine at the University of Texas Medical Branch, Galveston, a Rehabilitation Clinic in connection with the John Sealy Hospital was dedicated. Funds for the clinic were provided by the Monsanto Chemical Company, St. Louis, in appreciation of the services of the John Sealy Hospital in connection with the Texas City disaster last spring. Dr. Frank H. Krusen, professor of physical medicine, Mayo Foundation, Rochester, Minn., gave the dedication address.

WASHINGTON

Narcotic Violation.—Dr. Alphonse de Pierre-Hall, 302 South Thirteenth Street, Tacoma, pleaded guilty in the United States District Court in Tacoma to violation of the federal narcotic law and on January 2 was fined $1,500 and placed on probation for a period of six months.

Course in Applied Science.—The University of Washington School of Medicine, Seattle, has begun a course in the applications of basic sciences to disease. The course is arranged to bring together the physiologist, anatomist, biochemist, pharmacologist, pathologist and microbiologist with the clinicians. Classes, designed primarily for members of the resident staffs of hospitals who wish to qualify eventually for admission to specialty board examination, are being conducted each Thursday evening from 7 to 9 o'clock at Harborview Hospital Annex.

WEST VIRGINIA

Community Observes Doctor's Anniversary.—Dr. Edward L. McElfresh, Point Pleasant, completed fifty-five years of medical practice in Mason County on March 5, amidst a countywide observance of his anniversary. A program was arranged by the citizens of Point Pleasant and Mason County for the afternoon of March 7, and was attended by Dr. McElfresh's confreres from Mason and adjoining counties. In his honor a biographic sketch was read in all the schools of Mason County on March 5, pointing out the rigors of his pioneer practice and his modesty and devotion to duty throughout his fifty-five years of practice.

HAWAII

Annual Report of Board of Health.—Deaths from acute communicable diseases in the Territory of Hawaii reached an all time low in the fiscal year ending June 30, 1947, in spite of a rapidly expanding population. The tuberculosis death rate, after continuing at about 55 per hundred thousand population for several years, dropped to 49. However, the incidence of some communicable diseases showed an increase over the previous year: whooping cough from 9 to 616 cases; mumps from 277 to 597; chickenpox from 789 to 2329; typhus from 70 to 82 and poliomyelitis from 12 to 36. The leading cause of death is heart disease and the second is cancer. The population of the territory as of June 30, 1947 was estimated at 525,477, an increase of 1.2 per cent over the previous year. The crude mortality rate was six deaths per thousand population, the same as for 1946. The infant mortality rate for the territory was 31.2 per thousand live births, while it was 36.1 for the U. S. registration area in 1946. The maternal death rate for the territory dropped from 1.5 per thousand live births to 1.2 in 1947, the lowest ever recorded in Hawaii.

Child health conferences were held at regular intervals in one hundred and eighteen different locations throughout the territory and were participated in by fifty-one physicians, 5,608 infants, and 6,137 preschool children. Maternal health conferences were held at forty different centers by twenty-eight different physicians and were attended by 1,352 women.

The Bureau of Crippled Children had 2,305 crippled children under 21 years of age on the register, of whom 1,249 received some type of service from the bureau. During the year 382 new admissions were made to the register and 151 were discharged as cured, overaged or diseased. Fourteen traveling clinics which were held by the psychiatrist for the Bureau of Mental Hygiene served 359 patients and rendered 199 consultations concerning patients.

Human plague for the second successive year was not reported in the territory; however, 5 plague infections, 1 rodent, 1 mass flea inoculation, and 3 mass tissue inoculations were reported in the Hamakua district, the lowest number of plague infections reported in this area since 1932. One rodent plague infection was found on the island of Maui.

The Territorial Board of Health was designated by the governor as the agency to carry out the purposes of the new federal hospital survey and construction act; later Dr. William B. Meister, colonel, U. S. Army (retired), was employed to administer the act for the territory.

The total expenditure by the health department during the year was $1,942,954.99, of which $487,846.56 came from federal funds. The president of the Board of Health was Dr. Charles J. Wilbar Jr.

GENERAL

Florida Cited for Progress of Health Program.—Florida's public health program has been recognized by the Commonwealth Fund as making the "liveliest progress" of the six states receiving financial aid from the fund last year. The other states were Tennessee, Mississippi, Oklahoma, Louisiana and Kentucky. Florida now has sixty-two counties with local health departments.

Society for Prevention of Blindness.—The National Society for the Prevention of Blindness, Inc., will hold its annual conference at the Radisson Hotel, Minneapolis, April 5-7. Subjects under discussion include public health responsibility for eye health, vision education, organizing the community for sight conservation, industrial eye care, scientific advances in prevention of blindness and education of the exceptional child.

Resolution Approves Nurse Anesthetists.—The Board of Regents of the American College of Surgeons, at a meeting on February 22, adopted a resolution commending the services of nurses who have had special training in the administration of anesthetics and recommending the continuance of training courses in this field for nurses. The American College of Surgeons is of the opinion that, in view of the inadequacy in number of physician anesthesiologists and the splendid record of achievement of nurse anesthetists, institutions engaged in the training of nurses for this purpose should be encouraged to continue their program.

The Louis Livingston Seaman Fund.—The New York Academy of Medicine announces the availability of the Louis Livingston Seaman Fund for the furtherance of research in bacteriology and sanitary science. There is $1,200 available for assignment in 1948. This fund is provided by the terms of the will of the late Dr. Louis Livingston Seaman and is administered by a committee of the New York Academy of Medicine under the following conditions: 1. The committee will receive applications either from institutions or individuals up to April 15, 1948. Communications should be addressed to Dr. Wilson G. Smillie, chairman of the Louis Livingston Seaman Fund, 1300 York Avenue, New York, 21. The fund will be expended only in grants for investigation or scholarships for research in bacteriology or sanitary science. The expenditures may be made for securing of technical help, aid in publishing original work and purchase of necessary books or apparatus.

FOREIGN

Germany's Only Cyclotron.—The only practical cyclotron in Germany, according to David Nichol, foreign correspondent for the *Chicago Daily News*, has stood idle at the Kaiser-Wilhelm institute for more than two years; its use, however, was authorized recently by the four power Allied Control Council in Berlin. The cyclotron has been repaired and is expected to begin operations in March to produce for German physicians radioactive substances for research in the study and treatment of certain diseases; also to conduct basic research on methods of handling and using radioactive isotopes. The Heidelberg cyclotron is small compared with the new cyclotron being developed in the United States. It is said to command a maximum of about 12,000,000 volts, while the newest American cyclotrons are many times as powerful.

Deaths

Henry Fernand Ader ⊕ New Orleans; born in New Orleans, March 7, 1884, Medical Department of Tulane University of Louisiana, New Yrleans, 1906; member of the city board of health; assistant surgeon in the U. S. Public Health Service during World War I, serving as director of the bureau of venereal diseases for the state of Louisiana; at one time on the faculty of the New Orleans Polyclinic; from 1927 to 1929 member of the faculty of the Presbyterian Hospital School for Nurses, teaching diseases of the ear, nose and throat; formerly visiting surgeon, ear, nose and throat service of the New Orleans Hospital and Dispensary for Women and Children, visiting surgeon chief of ear, nose and throat service at the Presbyterian Hospital; on the staff of the Charity Hospital; chief of the ear, nose and throat department of the French Hospital, where he died Dec. 28, 1947, aged 63, of myocarditis.

William Henderson Marshall ⊕ Flint, Mich.; born in Brampton, Ontario, Canada, March 24, 1874; Trinity Medical College, Toronto, Canada, 1901; past president of the Northern Tri-State Medical Association; past president and secretary of the Genesee County Medical Society; past president of the Michigan Trudeau Tuberculosis Society; fellow of the American College of Physicians; for six years a member of the Michigan State Board of Registration in Medicine; served during World War I; for fifteen years chief of the medical service at the Hurley Hospital, where since 1938 he had been director emeritus of the department of internal medicine, and where he died January 8, aged 73, of heart disease.

Thomas J. Crowe, Dallas, Texas; born in New York June 18, 1861; Homeopathic Medical College of Missouri, St. Louis, 1887; for many years secretary of the Texas State Board of Medical Examiners, of which he was a past president; past president of the Federation of State Medical Boards of the United States; served as a member of the National Board of Medical Examiners; formerly chairman of the city board of health; past president of the Texas Homeopathic Medical Association; affiliated with the Baylor University and Parkland hospitals; died January 1, aged 86, of heard disease.

Henry J. Gramling ⊕ Dousman, Wis.; St. Louis College of Physicians and Surgeons, 1899; past president of the Milwaukee County Medical Society; for many years a member and at one time secretary of the state board of medical examiners; formerly councilor of the twelfth district of the State Medical Society of Wisconsin; served during World War I; formerly on the faculty of Marquette University School of Medicine; affiliated with St. Luke's Hospital in Milwaukee, where he was chief of staff for many years; died Dec. 10, 1947, aged 73, of injuries received in an automobile accident.

Fred Taylor Andrews, Bay City, Mich.; Detroit College of Medicine and Surgery, 1918; member of the American Medical Association; served as director of the Bay County Health Department; formerly associated with the Fisher Body Division of the General Motors Corporation in Lansing; an officer during World War I; president of the Bay County Society for Crippled Children; affiliated with Mercy Hospital and General Hospital, where he died Dec. 21, 1947, aged 58, of carcinoma of the brain.

Robert E. Flood, Gladwin, Mich.; Louisville (Ky.) Medical College, 1897; served as director of the Tri-County Health Department; affiliated with the James Decker Munson Hospital in Traverse City; died Dec. 7, 1947, aged 77, of coronary occlusion.

John Andrew Freese, Detroit; Harvard Medical School, Boston, 1907; member of the American Medical Association died recently, aged 71.

Samuel Friedman ⊕ New York; Bellevue Hospital Medical College, New York, 1895; member of the National Gastroenterological Association; died Dec. 14, 1947, aged 73, of coronary thrombosis.

Edwin Motley Fuller ⊕ Bath, Maine; Medical School of Maine, Portland, 1904; member of the New England Roentgen Ray Society; fellow of the American College of Surgeons; instrumental in the founding and president of the medical staff of Bath Memorial Hospital; died Dec. 2, 1947, aged 67

William Henry Gambill, Centralia, Ill.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1910; member of the American Medical Association; served during World War I; past president of the Marion County Medical Society and the Centralia Township High School Board; affiliated with St. Mary's Hospital; served as chairman of the advisory board of the Illinois State Department of Conservation; died Dec. 14, 1947, aged 65, of coronary thrombosis.

Sidney Brittcn Goff ⊕ Eaton Rapids, Mich.; Rush Medical College, Chicago, 1931; served during World War II; died suddenly, Dec. 27, 1947, aged 48.

Mark M. Kerr, Miami, Fla.; American Eclectic Medical College, Cincinnati, 1894; died recently, aged 87.

Robert Edward Longino, Biloxi, Miss.; University of Nashville (Tenn.) Medical Department, 1901; formerly state sanitary inspector and health officer of Coahoma County; died Dec. 18, 1947, aged 69.

William Major ⊕ Peoria, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1901; past president of the Peoria Medical Society; affiliated with Proctor Hospital; died in St. Francis Hospital Dec. 24, 1947, aged 74, of carcinoma of the urinary bladder.

Gottlieb Joseph Marum ⊕ Greenville, Miss.; Universität Köln Medizinische Fakultät, Köln, Prussia, Germany, 1919; died Dec. 19, 1947, aged 54, of heart disease.

Gilbert Lewis McBee ⊕ Pendleton, Ore.; University of Oregon Medical School, Portland, 1926; fellow of the American College of Surgeons; past president of the Umatilla County Medical Society; member of the board of education in 1946 and 1947; affiliated with St. Anthony's Hospital, where he died Dec. 22, 1947, aged 45, of carcinoma.

Robert Lyness McCready ⊕ New York; Columbia University College of Physicians and Surgeons, New York, 1907; formerly professor of gynecology and obstetrics at the New York Polyclinic Medical School and Hospital; specialist certified by the American Board of Obstetrics and Gynecology, Inc.; fellow of the American College of Surgeons; for many years affiliated with the Lenox Hill Hospital; died Dec. 14, 1947, aged 63, of cerebral hemorrhage.

Thomas Edward McGurk ⊕ Cape Girardeau, Mo.; St. Louis University School of Medicine, 1925; served on the staffs of the Missouri Pacific and St. Mary's hospitals in St. Louis; died Dec. 1, 1947, aged 45, of injuries received when his automobile struck a bridge abutment.

Florence Jess Correll McKenna, Los Angeles; State University of Iowa College of Medicine, Iowa City, 1910; died Dec. 22, 1947, aged 60, of cerebral hemorrhage.

Ocy May Crawford Johannes McKinley ⊕ Cleveland; University of Pittsburgh School of Medicine, 1926; a member of the board of trustees of Booth Memorial Hospital and the Woman's Hospital, where she died Dec. 17, 1947, aged 51, of carcinoma of the cervix uteri.

William Henry McLaughlin, Providence, R. I.; Dartmouth Medical School, Hanover, N. H., 1894; member of the American Medical Association; served on the school committee; affiliated with St. Joseph's Hospital; died Dec. 6, 1947, aged 78, of valvular heart disease.

Philip Howard Pettay, Flushing, Ohio; Starling-Ohio Medical College, Columbus, 1910; member of the school board; served as a physician for the Baltimore and Ohio Railroad; affiliated with the Martins Ferry (Ohio) Hospital; died recently, aged 71, of cerebral hemorrhage.

Eleanor L. Scull, Naples, Fla.; Woman's Medical College of Pennsylvania, Philadelphia, 1898; died Dec. 18, 1947, aged 81.

Daniel Joseph Sullivan Manchester, N. H.; Tufts College Medical School, Boston, 1916; fellow of the American College of Surgeons; died Dec. 16, 1947, aged 56.

Harvey E. Tucker, Lee's Summit, Mo.; Eclectic Medical University, Kansas City, 1901; retired druggist; died Dec. 9, 1947, aged 80.

Foreign Letters

PARIS

(From Our Regular Correspondent)

Feb. 20, 1948

Recent Researches On Synthetic Antihistaminics

Professor Pasteur Vallery-Radot's service at the Broussais Hospital conducts research on allergy and synthetic antihistaminic drugs. After conducting experiments, Drs. B. Halpern, J. Hamburger and S. Cruchand have reported that previous injection of 3,277 R.P. (N-(beta-dimethylamino- -Methyl -ethyl) phenothiazine) prevents, in 100 per cent of cases, acute pulmonary epinephrine-induced edema in rabbits. When given following the onset of edema, the drug appears curative. This same effect was noted in rabbit lung edema induced by chloropicrin (a war gas, trichloronitromethane) in which the drug appeared equally curative. Study of the use of the drug against other war gases is continuing.

In studies with the same drugs, Halpern and Laubsher reported that in 8 of 10 patients with allergic conditions there was an extremely great increase in capillary resistance beginning one to two hours after injection and persisting up to forty eight hours. In nonallergic patients the antihistaminic drugs did not appreciably modify capillary resistance.

Drs. Halpern, Perrin and Dews reported work on the local anesthetic powers of certain antihistaminic agents. They reported that compounds 3,300 R.P. and 3,376 R.P. show local anesthetic power four to six times greater than that of cocaine. They concluded from this that certain local effects of these drugs may be attributed to their anesthetic rather than their antihistaminic properties.

Streptomycin

At the Hospital for Sick Children, Professor R. Debre has instituted routine streptomycintherapy for tuberculous meningitis in children comprising one week of 100,000 units of the agent per kilogram of body weight per day parenterally plus two intrathecal injections of 50,000 to 100,000 units. After the first week, the patient receives 50,000 units per kilogram per day until cured. Treatment is suspended only after the disappearance of all pathologic signs. In 5 children with neurosurgical complications, surgical intervention disclosed a leptomeningitis or a pachymeningitis. A sixth child had a large tubercle near the chiasma. Operative intervention was highly successful in 2 cases. Early diagnosis was considered of utmost importance in predetermining the result of treatment. Of 100 children treated by Professor Debre, 46 have been successfully cured.

Ch. Mattei, Marseilles, presented results of treatment of 130 patients with streptomycin. Among these, of 22 cases of serious tuberculous laryngitis, 4 recovered and 17 were greatly improved. Of 20 patients with tuberculous meningitis, 17 recovered and 3 died. Pulmonary cavities associated with miliary or other tuberculosis closed rapidly during the course of intramuscular treatment with streptomycin. Relapses among all patients were frequent when insufficient dosage was employed. The author believed that neurotropism might well be responsible for the frequent appearance of neurologic complications from use of streptomycin. Such accidents were compared with similar complications which occur during gold therapy.

Congresses

The twelfth Congress of French-Speaking Pediatricians is scheduled in Paris from May 10 to 15, 1948 with Professor Edmond Lesne, member of the National Academy of Medicine, presiding. Subjects on the program include (1) toxic syndrome of nurslings: (A) etiologic, pathologic and therapeutic study by J. Levesque, Paris; (B) biologic study by Professor Fanconi, Zurich; (2) bronchial dilation in children: (A) anatomic and radiologic study, R. A. Marquezy and P. Renault, and (3) disorders of the function of speech in children, C. Launay, Paris. Full information may be obtained by corresponding with the general secretary, Dr. A. Marquezy, 16 Avenue Georges V, Paris (8).

The Congress of Longevity will be held under the auspices of the Vittel Medical Society at Vittel, June 12-13, 1948, with P. Joannon, professor of hygiene and preventive medicine at the Paris Faculty, presiding. Principal items of discussion relate to adult hygiene and the physiopathology of senescence, diseases of middle and old age, and improvements of sanitary and social hygiene measures necessary to extend life expectancy. The congress has been divided into several sections, which include (1) biology and clinics, (2) hygiene and general therapeutics and (3) statistics and sociology. Communications regarding the congress should be addressed to the general secretaries, Dr. Boigey at Vittel (Vosges), or Professeur Agrege M. Deparis, Laboratory of Hygiene of the Paris Faculty of Medicine, 21 Rue de l'Ecole de Medecine, Paris.

MADRID

(From Our Regular Correspondent)

Jan. 12, 1948.

The Midbrain-Pituitary Regulation of Carbohydrate Metabolism

At the Digestive Pathology and Nutrition Congress held in Spain, Dr. J. Andreu Urra, professor at Seville University spoke on The Midbrain-pituitary regulation of carbohydrate metabolism. He summarized his research since 1935, which was started in collaboration with Grünthal and Stryeck, studying the physiology of the midbrain-pituitary region. He mentioned the experimental and clinical facts which proved the part of the midbrain in the regulation of carbohydrates, saying that for the time being this regulation cannot be localized in any well defined cell group and accepting Hess's two anatomicophysiologic zones: the ergotrope, or sympathetic, and the trophotrope, or parasympathetic. While the posterior lobe of the pituitary has little or no importance as regards carbohydrate metabolism, the anterior lobe intervenes decisively, exercising its action through the various factors whose unity or plurality is still not clear.

The author and his collaborators have not been able to prove any variations in the regulation of glycohemia by acting through the optic midbrain-pituitary system. Finally, studying the main arguments in favor of the insular pathology of diabetes, he expressed the opinion that the pituitary factors are fundamental in this conection and that "in diabetes mellitus we must always accept the existence of an insulin deficiency, which is surely constitutional, and whose manifestation in the form of diabetes will be easier understood when to the pancreatic failure there is added a pituitary decompensation." In the field of therapeutics he advised going on with radiotherapy of the pituitary. In his experience the gonadal hormones have proved useless. This report of Professor Andreu's school enhances the reputation of the Seville Faculty of Medicine and is a tribute to the school of Professor M. Banueios (Valladolid), where Dr. Andreu was trained.

National Cardiology Congress

The second National Cardiology Congress was held in Barcelona Dec. 11-14, 1947. The inaugural session was held in the assembly hall of the Royal Academy of Medicine, the old chair ofanatomy in which the famed Ginbernat once taught. In the audience were the civil governor of Barcelona, the president of congress, Professor A. Pedro y Pons, Dr. J. Framis de Mena, secretary of the Organizing Committee of the congress, and other notable persons. Dr. A. Crespo Alvarez lectured on the social aspect in diseases of the circulatory system and suggested regulations for the Spanish Cardiology Society and the campaign to help patients studied jointly by the members of the committee of the society.

On December 12 at the Doctors' Club, Professor L. Trias

de Bes, director of the Infectious Diseases Hospital of Barcelona, read the first paper, on "Acute and Subacute Endocarditis." The report was warmly applauded in tribute to the author and his collaborators: Professor J. Sanchez Lucas, author of a complete anatomicopathologic study of endocarditis; Dr. Foz Tena, who investigated the bacteriologic aspects of endocarditis; Dr. Gras Riera, entrusted with the biologic aspects, especially of the plasmatic syndrome, and Dr. Cabre, who studied the dermatologic features. They came to the conclusion that there are two types of endocarditis of slow malignant evolution: (1) nonbacteremic, in which prognosis is more serious and which the authors suspect may be the evolutive malignant rheumatic endocarditis mentioned by some classic authors, and (2) bacteremic, including all forms of bacterial endocarditis of a subacute nature, whatever the germ that produces them. The evolution of each of these types is totally different, since the latter responds well to treatment with antibiotics while the former is nearly always fatal. Drs. J. Jimenez Diaz, A. Pedro y Pons, M. Soriano Jimenez, J. Gilbert Queralto, M. Beltran Baguena, T. Alday, J. Lamelas, F. Vega Diaz and many others took part in the debate on this report. In the afternoon Dr. Juan Lopez Brenes, a collaborator of Professor C. Jimenez Diaz, read a report on "Myocardial Infarct," in which he set forth his wide experience of the subject with electrocardiographic documentation. This report was also discussed by Drs. Adrio, Azpitarte, Vela, Benot Lozano, Bozal, Gonzalez Suarez, Codina Altes, Pijoan, Bravo, Clavera, Juncadella, Cornella, Soriano, Ciscar, Balcells, Cuellar, Duque Sampayo, Ortiz, Perez Gonzalez, Vega Diaz, and Roda. On December 13 Dr. A. Azpitarte from Granada read the third report on "Acute Tachycardias." The author reviewed all aspects of tachycardiac paroxysmal arrhythmias. In the afternoon a lecture was given by Dr. C. Jimenez Diaz, of the Madrid Faculty of Medicine, on "Arterial Hypertension." He submitted a report on the subject at the First National Cardiology Congress three years ago. After this a lecture was given by Dr. J. Lamelas, head of the cardiology department of the Valdecilla (Santander) on "Cardiopathies and Pregnancy." Later the Spanish Cardiology Society held a meeting at which Dr. J. López Brenes spoke of the work done during the last three years and the financial difficulties which had to be overcome. The committee was then reelected for the next three years. The number of members attending the congress was one hundred and sixty-eight, besides one hundred and twenty-five collaborators. Visits were made to the National Museum of Montjuich, to the "Spanish Village" of Barcelona (a quarter especially devoted to displaying the customs and dresses of the various Spanish regions), a gala performance at the Liceo theatre, receptions and a farewell lunch at the Windsor Restaurant, where Profesor A. Pedro y Pons again spoke, wish them farewell in a few stirring words. The second National Cardiology Congress was an immense success.

The Spanish Journal of General and Applied Psychology

A new journal, entitled *Revista de Psiocologia General y Aplicada*, has just started publication in Madrid under the editorship of Dr. Jose Germain, who was director of the National Institute of Psychotechny until the end of the civil war. The object of the review is to present psychologic questions in all their amplitude, from those touching on philosophy to their more concrete applications in medicine and pedagogy, industry, and economic and social sciences. The first three issues of the new journal have already appeared.

BELGIUM

(From Our Regular Correspondent)

Liége, Feb. 18, 1948.

Intoxication by Aromatic Hydrocarbons

In the Belgian review of Social and Occupational Medicine Merlevelde, who is connected with a plant manufacturing chemical products, explains the present status of intoxication by hydrocarbons. His studies of the physiopathology of amino derivatives show that they exert a special action on the blood and produce anemia. They act equally on the nervous system and skin and secondarily on the bladder. Merlevelde does not limit himself to a report on the classic signs of poisoning by aniline; he investigated variations in the iron content of the plasma; he has studied the action of the aromatic products on the sedimentation speed and has investigated the importance of ascorbic acid on these poisonings. He has established that the resistance of the organism to benzene is increased by prophylactic administration of ascorbic acid. Merlevelde has verified these factors in workers who are exposed to aromatic products and their derivatives, and he has completed his investigations by experiments on guinea pigs. It seems that ascorbic acid acts as an antidote to these toxic substances.

Merlevelde takes up the question of the treatment of aniline poisoning, the methods of chemical detection and the various measures of technical and personal prophylaxis which he found expedient to employ.

Epidemic of Oil Pustules

Malter presented before the Belgian Society of Occupational Medicine an interesting contribution on lesions caused by industrial oil. He observed a veritable epidemic of pustules in different metallurgical factories in the region of Liége. This disorder appeared, particularly during the war period, due to the use of oils of inferior quality or the reuse of oils. Malter describes the industrial operation which gives rise to these disorders with the passing and repassing of the oil from the machine to the reservoir. He shows how this oil becomes infected by contact with skins previously infected with staphylococcic lesions. Specimens of oil obtained at the level of the machines revealed that they contain more than 90,000 particles of iron per cubic millimeter and staphylococci in large numbers.

In reviewing the literature, Malter thinks the authors have not considered all the factors in this disorder. In his opinion it is necessary to consider the mechanical factor due to the presence of metallic particles, a chemical factor which varies according to the nature of the oils used (mineral oils, coal oils or vegetable oils), an infectious factor and finally a human factor. He thinks that only chemical disinfection of the oils by some nonirritating agent can give complete satisfaction.

Biopsy of Gastric Mucosa Under Gastroscopic Control

At the Belgian Society of Gastroenterology, Carmena D'Almeida of Paris demonstrated that a flexible biopsy forceps can be introduced simultaneously with a gastroscope that has an improved optic attachment, the entire apparatus being enclosed in a thin rubber cover. The forceps is guided by silk thread traction under visual control. Specimens obtained will permit distinction between certain benign and cancerous tumors, and this will be a guide for more adequate therapy: It will be interesting to know the histologic aspect of the antral mucosa in pernicious and other anemias; in benzene gastritis and in the gastritis of arc welders.

Vision and Tobacco

Before the Society of Legal Medicine of Belgium, Hambresine and Schepens pointed out that amblyopias due to tobacco were frequent in Belgium during the war and that in the invaded and besieged regions one still finds smokers with diminished vision. Various authors think that the lesion in question is due to an intoxication due to both alcohol and tobacco. The only absolute diagnostic element is a peripheral scotoma which can be easily seen by means of the screen of Bjerrum. This scotoma characteristically presents one or two or even more extremely dense zones. The constituent of tobacco that provokes this visual disturbance is not known. The treatment is simple. It is sufficient to abstain from tobacco, but often improvement is not evident until the patient has abstained from tobacco for several weeks.

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

NATIONAL BOARD OF MEDICAL EXAMINERS EXAMINING BOARDS IN SPECIALTIES

Examinations of the National Board of Medical Examiners and the Examining Boards in Specialties were published in THE JOURNAL, March 13, page 796

BOARDS OF MEDICAL EXAMINERS

ARIZONA:* Examination. Phoenix, April 6-7. Endorsement. Phoenix, April 10. Sec., Dr. J. H. Patterson, 826 Security Bldg., Phoenix.

ARKANSAS:* *Examination.* Little Rock, June 3-4. Sec., Medical Board of the Arkansas Medical Society, Dr. L. J. Kosminsky, Texarkana. *Eclectic:* Little Rock, June 3. Sec., Dr. C. H. Young, 1415 Main St., Little Rock.

CALIFORNIA: *Oral.* San Francisco, June 5-6; Los Angeles, Aug. 7-8. *Written Examination.* Los Angeles, Aug. 9-12. *Oral and Clinical Examination for Foreign Graduates.* San Francisco, June 6. Sec., Dr. Frederick N. Scatena, 1020 N Street, Sacramento 14.

COLORADO:* *Examination.* Denver, June 21-23. Final date for filing application is June 5. *Endorsement.* Denver, April 6. Final date for filing application is March 20. Sec., Dr. J. B. Davis, 831 Republic Bldg., Denver.

CONNECTICUT:* *Examination.* March 9-10. Sec., Dr. Creighton Barker, 258 Church St., New Haven. *Homeopathic Examination.* Derby, March 9-10. Sec., Dr. J. H. Evans, 1488 Chapel St., New Haven.

DELAWARE: *Examination.* Dover, July 13. *Endorsement.* Dover, July 22. Sec., Dr. J. S. McDaniel, 229 S. State St., Dover.

HAWAII: Examination. Honolulu, July 12-15. Sec., Dr. S. Doolittle, 881 S. Hotel St., Honolulu.

IDAHO: Boise, July 13-15. Sec., Bureau of Occupational Licenses, Miss Estella S. Mulliner, 355 State House, Boise.

ILLINOIS: Chicago, April 6-8. Supt., Dept. of Registration and Education, Mr. Fred W. Ruegg, Springfield.

INDIANA: *Examination.* Indianapolis, June 1948. Sec., Board of Medical Registration and Examination, Dr. Paul R. Tindall, K of P Bldg., Indianapolis.

KANSAS: Kansas City, June 9-10. Sec., Board of Medical Registration & Examination, Dr. J. F. Hassig, 905 N. 7th St., Kansas City.

KENTUCKY: *Examination.* Louisville, June 16-18. Sec., Dr. P. E. Blackerby, 620 S. 3d St., Louisville.

MARYLAND: *Medical Examination.* Baltimore, June 15-18. Sec.-Treas., Dr. Lewis P. Gundry, 1215 Cathedral St., Baltimore. *Homeopathic Examination.* Baltimore, June 15-16. Sec., Dr. J. A. Evans, 612 W. 40th St., Baltimore.

MINNESOTA:* Minneapolis, April 20-22. Sec., Dr. J. F. DuBois, 230 Lowry Medical Arts Bldg., St. Paul.

MISSISSIPPI: Jackson, June 1948. Asst. Sec., State Board of Health, Dr. R. N. Whitfield, Jackson.

MISSOURI: *Examination.* St. Louis, May 24-26. Final date for filing application is April 24. Exec. Sec., Mr. John A. Hailey, State Capitol Bldg., Jefferson City.

MONTANA: Helena, April 5-7. Sec., Dr. O. G. Klein, First Nat'l Bank Bldg., Helena.

NEBRASKA:* *Examination.* Omaha, April 5-7. Dir., Mr. Oscar F. Humble, Room 1009 State Capitol Bldg., Lincoln 9.

NEVADA: Carson City, May 3. Sec., Dr. G. H. Ross, 215 N. Carson St., Carson City.

NEW JERSEY: *Examination.* Trenton, June 15-17. Sec., Dr. E. S. Hallinger, 28 W. State St., Trenton.

NORTH CAROLINA: *Endorsement.* Pinehurst, May 4. Sec., Dr. Ivan Procter, 226 Hillsboro St., Raleigh.

NORTH DAKOTA: Grand Forks, July 6-9. Sec., Dr. G. M. Williamson, 4½ S. 3rd St., Grand Forks.

OHIO: *Endorsement.* Columbus, April 6. Sec., Dr. H. M. Platter, 21 W. Broad St., Columbus 15.

OKLAHOMA:* Oklahoma City, June 2-3. Sec., Dr. Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON:* *Endorsement.* Portland, May 7-8. Final date for filing application is April 23. Sec., Miss L. M. Conlee, 608 Failing Bldg., Portland.

PENNSYLVANIA: *Examination.* Philadelphia & Pittsburgh, July. Act. Sec., Bureau of Professional Licensing, Mrs. M. G. Steiner, 351 Education Bldg., Harrisburg.

RHODE ISLAND:* *Examination.* Providence, April 1-2. Chief, Mr. Thomas B. Casey, 366 State Office Bldg., Providence.

SOUTH CAROLINA: *Written Examination.* Columbia, June 21-23. *Endorsement.* April 5. Sec., Dr. N. B. Heyward, 1329 Blanding St., Columbia.

SOUTH DAKOTA:* Pierre, July 20-21 * Sec., Dr. Gilbert Cottam, Capitol Bldg., Pierre.

TENNESSEE:* *Examination.* Memphis, March 24-25. Sec., Dr. H. W. Qualls, 1635 Exchange Bldg., Memphis.

UTAH: *Examination.* Salt Lake City, June, 1948. Asst. Dir., Department of Registration, Miss Rena B. Loomis, 324 State Capitol Bldg., Salt Lake City.

VIRGINIA: *Examination.* Richmond, June 18-19. *Endorsement.* Richmond, June 17. Sec., Dr. K. D. Graves, 306 Medical Arts Bldg., Roanoke.

WEST VIRGINIA: Charleston, April 5-7. Comm., Public Health Council, Dr. N. H. Dyer, State Capitol Bldg., Charleston.

WISCONSIN:* Milwaukee, June 29-July 1. Sec., Dr. C. A. Dawson, Tremont Bldg., River Falls.

WYOMING: *Examination.* Cheyenne, June 7. Sec., Dr. G. M. Anderson, Capitol Bldg., Cheyenne.

* Basic Science Certificate required.

BOARDS OF EXAMINERS IN THE BASIC SCIENCES

ARKANSAS: Little Rock, May 4. Sec., Mr. L. E. Gebauer, 1002 Donaghey Bldg., Little Rock.

DISTRICT OF COLUMBIA: *Examination.* Washington, April 19-20. Sec., Dr. G. C. Ruhland, 4130 Municipal Bldg., Washington.

FLORIDA: *Examination.* June 5. Final date for filing application is May 23. Sec., Mr. M. W. Emmel, Univ. of Florida, Gainesville.

IOWA: Des Moines, April 13, July 13, Oct. 12. Sec., Dr. Ben H. Peterson, Coe College, Cedar Rapids.

MICHIGAN: *Examination.* Ann Arbor and Detroit, May 14-15. Sec., Miss Eloise LeBeau, 101 N. Walnut St., Lansing 15.

MINNESOTA: *Examination.* Minneapolis, April 6-7. Sec., Dr. Raymond N. Bieter, 105 Millard Hall, Univ. of Minnesota, Minneapolis.

NEBRASKA: *Examination.* Omaha, May 4-5. Dir., Bureau of Examining Boards, Mr. Oscar F. Humble, Room 1009 State Capitol Bldg., Lincoln 9.

NEW MEXICO: *Examination.* Santa Fe, March 21. Sec., Miss Marguerite Kilkenny, 114 E. Marcy, Santa Fe.

OKLAHOMA: Oklahoma City, April 2. Sec., Dr. Frank Clinton Gallaher, 813 Braniff Bldg., Oklahoma City.

OREGON: *Examination.* Portland, June 19. Sec., Basic Science Examining Committee, Mr. C. D. Byrne, Univ. of Oregon, Eugene.

SOUTH DAKOTA: *Examination.* Vermillion, June 4-5. Sec., Dr. G. M. Evans, 310 E. 15th St., Yankton.

WISCONSIN: *Examination.* Madison, April 3. Sec., Dr. W. H. Barber, Scott & Watson Sts., Ripon.

Medical Motion Pictures

FILM REVIEW

RETURN TO ACTION. 16 mm., black and white, sound 725 feet (1) reel, showing time nineteen minutes. Produced in 1946 for the British Ministry of Labour, London, England. Procurable on loan from British Information Service, 30 Rockefeller Plaza, New York 20 or Local Office.

This excellent film on vocational rehabilitation describes the extremely well-organized program which has been developed in England for the vocational rehabilmtation of disabled persons. The work at the Vocational Rehabiltation Center at Egham is shown; here successive groups of disabled men are trained vocationally to assume again their places in civilian life. The script centers around the progressive rehabilitation of a man whose lower extremity was amputated and who proceeds from the stage of despair because of his disablement through successive stages to reemployment. First he goes to Egham for vocational rehabilitation, then t c the government training center at Stowe and finally to the Devon residential training center. At last he is placed in a suitable posintion in industry and happily reemployed.

The filming is of good quality, the narration is excellent and the picture will interest anyone primarily concerned with rehabilitation of the seriously disabled. While there is little of a medical nature in this film physicians should see it because it indicates clearly how modern methods of industrial and vocational rehabilitation can restore even seriously handicapped persons. This Film could well be used as a supplement to the several excellent films on physical rehabilitation which have been prelent films on physical rehabilitation which have been prepared recently.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1938 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted.

American Journal of Medical Sciences, Philadelphia

214:465-584 (Nov.) 1947

Relapse of Patients with Pernicious Anemia Receiving Folic Acid. O. C. Hansen-Pruss.—p. 465.
Diagnostic Value of Sternal Bone Marrow Puncture in Polycythemia Vera. I. H. Manning Jr.—p. 469.
*Anemia and Its Relation to Diaphragmatic Hernia. J. O. Ritchey and H. J. Winsauer.—p. 476.
*Prolonged Incubation Period as Epidemiologic Principle of Infectious Hepatitis and Homologous Serum Jaundice. W. L. Aycock and W. F. Oren.—p. 483.
*Caronamide, Compound That Inhibits Penicillin Excretion by Renal Tubules, Applied to Treatment of Subacute Bacterial Endocarditis. W. P. Boger, C. F. Kay, S. H. Eisman and E. E. Yeoman.—p. 493.
Convulsive State in Diabetes. M. Ellenberg and H. Pollack.—p. 503.
Urinary Excretion of Amino Acids by Cystinuric Subject. H. L. Yeh, W. Frankl, M. S. Dunn and others.—p. 507.
Examination of Hypertensive Patient. M. Backer.—p. 513.
Infarction of Entire Pulmonary Lobe with Subsequent Aseptic Softening Causing Sterile Hemopneumothorax. A. J. Rawson and J. A. Cooke.—p. 520.
Significance of Clinical Findings in Cirrhosis of Liver: Study of 93 Autopsied Cases. J. Hoffman and J. R. Lisa.—p. 525.
Interference Between Inactive and Active Viruses of Influenza: V. Effect of Irradiated Virus on Host Cells. W. Henle, Gertrude Henle and Maria W. Kirber.—p. 529.
Cold Hemagglutinins in Sickle Cell Anemia. J. E. J. McSweeney, A. C. Mermann and P. F. Wagley.—p. 542.
*Propylthiouracil in Treatment of Hyperthyroidism. E. P. McCullagh, R. E. Hibbs and R. W. Schneider.—p. 545.
Use of Pyribenzamine in Prevention of Histamine-Induced Gastric Acidity and Headache and in Treatment of Hypersensitiveness to Cold. E. L. Perry and B. T. Horton.—p. 553.
Application of Immunologic Principles to Management of Hay Fever, Including Preliminary Report on Use of Freund's Adjuvant. Mary H. Loveless.—p. 559.
Rheumatoid Spondylitis. D. G. Pugh.—p. 568.

Anemia and Diaphragmatic Hernia.—Ritchey and Winsauer review 41 cases of diaphragmatic hernia, the records of which were found either in the medical records of the Indiana University Medical Center or in the files of the roentgenologic department. There were 27 females and 14 males, which is in accord with the accepted predominance of females over males. Thirty of the cases showed herniation of the stomach alone, the other 11 cases involving herniation of the stomach plus other abdominal viscera. The authors detected a secondary anemia in 11 of the 41 cases. This incidence of anemia is not as high as in some reported series, but is higher than in a number of other series. It tends to substantiate the fact that anemia in diaphragmatic hernia is often found as part of the disease and that it does not have to be associated with a history of gastrointestinal bleeding.

Prolonged Incubation: Infectious Hepatitis and Homologous Serum Jaundice.—Aycock and Oren show that in neutralization and protection tests in a number of virus infections having different incubation periods a portion of the animals inoculated with mixtures of virus and immune serum develop the disease following incubation periods that are longer than those resulting from inoculation with virus and nonimmune serum. Prolongation is proportionate to the length of the incubation periods of each of the several diseases. The degree of prolongation of the incubation period of homologous serum jaundice over that of infectious hepatitis is equivalent to that observed in other neutralization or protection tests. In the light of this epidemiologic principle it is suggested that the difference in the incubation periods of infectious hepatitis and homologous serum jaundice is due to differences in the manner of transmission of a single virus which involve admixture of virus with antibodies. The shorter incubation period, generally regarded as characteristic of infectious hepatitis, occurs when transmission of either of the two types of jaundice is accomplished by intranasal or oral administration or by contact (serum-free virus). The longer incubation period, regarded as characteristic of homologous serum jaundice, follows the transmission of either of the types of jaundice by the injection of serum containing virus. It is postulated that the prolongation of the incubation period of homologous serum jaundice over that of infectious hepatitis is the result of partial neutralization of the virus by admixture with serum containing antibodies of either the donor or recipient patient or by the in vitro action of serum that contains antibodies on the virus

Caronamide and Penicillin in Bacterial Endocarditis.—Boger and his co-workers found in preliminary clinical investigations that penicillin plasma concentrations were enhanced threefold to sevenfold by the oral administration of caronamide, and no serious toxic manifestations were observed. They treated a woman aged 51 with subacute bacterial endocarditis due to a strain of streptococcus resistant to penicillin and streptomycin by the intramuscular administration of penicillin and the oral administration of caronamide. In this patient, as in a control in whom the two substances were administered simultaneously, there was good correlation between the concentration of caronamide in plasma and the enhancing effect on concentrations of penicillin in plasma. The authors stress that even when the dosage employed is measured in millions of units per day, the plasma levels of penicillin can be elevated by the administration of caronamide. The effect of caronamide in the treatment of this patient was equivalent to the injection of additional millions of units of penicillin.

Propylthiouracil in Hyperthyroidism.—The use of propylthiouracil over a fourteen month period convinced McCullagh and his associates that the drug is decidedly superior to thiouracil in the treatment of hyperthyroidism. In 218 patients treated for an average of eight months and in some treated as long as fourteen months no cases of agranulocytosis were seen. Three minor reactions occurred, and four other reactions required the cessation of treatment. The drug is effective in the control of hyperthyroidism of all types except possible instances of acute crisis, in which its action is too slow. The hyperthyroidism of acromegaly may also be an exception. An effective dose in more than 95 per cent of patients has been 300 mg. per day. A smaller dose is effective in many cases; a larger dose has been required in less than 4 per cent. Iodine in doses as high as 30 mg. per day may be used concurrently with propylthiouracil. It will eliminate the thrill and bruit in diffuse glands and does not hinder the action of propylthiouracil.

American Journal of Surgery, New York

74:795-904 (Dec.) 1947. **Partial Index**

Perforating Wound of Pericardium. S. Z. Hawkes.—p. 797.
Demonstration at Operation of Sphincteric Action at True Gastric Stoma. C. S. Kennedy, R. P. Reynolds and M. O. Cantor.—p. 808.
Nontraumatic Perforation of Common Bile Duct. H. M. Gans and M. Reydman.—p. 811.
Congenital Megacolon Hirschsprung's Disease: Megacolon Treated by Segmental Resection. J. Hersh.—p. 815.
Foreign Body Perforation of Sigmoid Simulating Carcinoma. A. Meltzer and D. B. Hackel.—p. 824.
Endometriosis of Umbilicus. B. J. Weisband and C. Modica.—p. 827.
Plastic Reconstruction Following Third Degree Burn of Forearm. N. Brodie.—p. 834.
Reconstruction of Face and All Four Eyelids. O. S. Steinreich and A. Callahan.—p. 838.
Unusual Metastatic Manifestations of Breast Carcinoma: Cutaneous Hemorrhagic Metastasis. J. B. Herrmann and F. E. Adair.—p. 844.
Spontaneous Amputation of Fallopian Tube. F. M. Flickinger and J. C. Masson.—p. 850.
Cesarean Section Seven Years After Hemihysterectomy in a Bicornate Uterus. W. P. Smith.—p. 856.
Hyperparathyroidism and Pregnancy. D. W. Petit and R. L. Clark.—p. 860.
Intra-Abdominal Hemorrhage During Pregnancy. A. F. Lee.—p. 867.
Placenta Accreta. L. Rademaker, I. R. Hansen and R. La Rue.—p. 869.
Primary Ovarian Pregnancy of Four Months. P. D. Badia.—p. 874.
Replacement of Upper End of Femur with Fibular Graft. R. D. McClure and C. R. Lam.—p. 882.
Heredofamilial Cleft Foot Deformity: (Lobster-Claw Foot or Split Foot). H. W. Meyerding and J. E. Upshaw.—p. 889.
Danger Signal in Traumatic Anterior Dislocation of Hip. C. F. Goeringer.—p. 893
Simultaneous Occurrence of Multiple Primary Carcinomas Within Abdominal Cavity. K. B. Hanson and J. T. Crone.—p. 895.

American Journal of Tropical Medicine, Baltimore

27:663-798 (Nov.) 1947. Partial Index

*"Mal Del Pinto" or "Carate" and its Treatment with Chlorhydrate of 3-Amino-4 Oxiarsenbenzen (Mapharsen). G. Varela and C. Avila.—p. 663.
Factors That Influence Degree of Parasitemia in Ducks Infected with Plasmodium Lophurae. R. H. Rigdon and B. E. McCain.—p. 673.
*Plague: Survey of Recent Development in Prevention and Treatment of Disease. J. M. Ruegsegger and H. Gilchrist.—p. 683.
Method for Testing Ointments and Fabrics to Determine Their Effectiveness as Barriers to Schistosome Cercariae. R. E. Kuntz, M. A. Stirewalt and J. R. Buchheit.—p. 691.
Visceral Leishmaniasis Complicated by Severe Anemia—Improvement Following Splenectomy. J. H. Burchenal, R. F. Bowers and T. A. Haedicke.—p. 699.
Aedes Aegypti Control in Absence of Piped Potable Water Supply. P. F. De Caires.—p. 733.
Asymptomatic Toxoplasmosis. B. H. Kean and R. G. Grocott.—p. 745.

"Mal del Pinto;" Treatment by "Mapharsen."—Varela and Avila say that according to a 1934 census there were 270,049 persons with pinta, mal del pinto, or carate in Mexico. They estimate that in the rest of the Western Hemisphere, chiefly Colombia and Venezuela, there are approximately 500,000 persons infected with this disease. In 1938 a treponeme which has been designated as Treponema carateum, or Treponema herrejoni, was discovered in the lesions and lymph nodes of patients with pinta. The authors were able to grow T. carateum in anaerobic mediums, or on the chorioallantoic membrane, or in the yolk of fertilized eggs. The authors studied 805 patients with regard to the history of pinta in their parents. They found a somewhat higher incidence of pinta in persons whose parents had the disease than in those whose parents were free from it. Pinta usually begins with spots of desquamating erythema chiefly on the uncovered parts of the body. Later dyschromic lesions appear, which may be red, pink, blue and white. The red and blue lesions are distributed all over the body, whereas the white spots are mainly found on shoulders, elbows, hand, knees and feet. In nearly half of the patients pruritus exists during the dyschromic stage. Wassermann and Kahn reactions are frequently positive. The authors used oxophenarsine hydrochloride ("mapharsen") for treatment, administering 0.04 Gm. twice a week. The total number of injections was usually fifteen, although some were given only five. Several hundred patients were treated, but only 66 were observed for periods as long as a year. In 6 the lesions were not changed in aspect, and in the others only part of the hyperchromic spots disappeared.

Plague.—Ruegsegger and Gilchrist believe that an antiplague program should include (*a*) quarantine and isolation, (*b*) control of rodent populations, (*c*) emphasis on pulicidal measures, and (*d*) prophylaxis of the individual contacts. Effective therapeutic agents are now available. Serums have been developed, but the objection to all serums, expense and necessity for parenteral administration, applies to antiplague serum and may conceivably be its limiting factor. The sulfonamide drugs, particularly sulfadiazine, constitute the most effective therapeutic agents in plague. Suggestive confirmation of the curative effect of the sulfonamide compounds in human infections is accumulating. Streptomycin has been shown by Wayson and McMahon to be effective in curing plague in guinea pigs. The human clinical application awaits confirmation. Chu in discussing the current situation with regard to plague in China reported a unique incident which suggests a more hopeful prognosis for victims of pulmonic plague. A physician contracted pneumonitic plague while engaged in transferring virulent cultures in the laboratory. Sulfadiazine therapy was instituted in full doses on the second day of symptoms after the diagnosis had been confirmed culturally. On the fourth day and for several days thereafter streptomycin was also administered. The patient made an uneventful and complete recovery.

Illinois Medical Journal, Chicago

92:313-362 (Dec.) 1947

Surgical Treatment for Carcinoma of Esophagus. P. Thorek.—p. 329.
Early Ambulation in Surgical Patient. A. M. Vaughn, A. C. Guzauskas and F. A. Lagorio Jr.—p. 337.
Mental Aspects of Growth and Health. B. I. Beverly.—p. 341.
Diagnosis of Pulmonary Tuberculosis. G. H. Vernon.—p. 344.
Observations on Fracture Treatment. H. A. Sofield.—p. 346.
Indications for Lumbar Sympathectomy. G. De Takats.—p. 349.
Ambulatory Electric Shock Therapy in an Out-Patient Clinic. H. R. Johnson.—p. 351.

Indiana State Medical Assn. Journal, Indianapolis

40:1204-1330 (Dec.) 1947

Paradox of Psychoneurotic Malingering. A. R. MacLean.—p. 1223.
Correction of Chronic Sinusitis. J. J. Littell.—p. 1226.
Acute Ischemic Necrosis of Anterior Compartment Muscles of Leg. R. A. Royster.—p. 1229.
*Penicillin in Infectious Syphilis. H. L. Joseph, G. F. Kempf and G. W. Bowman.—p. 1232.
Stress Versus Predisposition in Combat Psychiatry. W. L. Sharp.—p. 1234.

Penicillin in Infectious Syphilis.—Joseph and his associates review observations on 263 patients with syphilis who were treated with penicillin in four different dosage schedules. There were 168 patients who received 2,400,000 Oxford units of sodium penicillin in aqueous solution, 20,000 units every three hours for fifteen days; 38 received 4,800,000 units, 40,000 units every three hours for fifteen days; and 47 had 9,600,000 units, 80,000 units every three hours for fifteen days. The fourth group, comprising 10 patients, received 9,600,000 units of calcium penicillin in peanut oil and beeswax, given by a single daily intramuscular injection of 600,000 units for sixteen consecutive days. Patients were followed clinically and serologically from one to eighteen months after treatment. The study is presented to indicate a trend that higher dosages are probably advisable. It is also suggested that the general practitioner use penicillin as an adjunct to regular arsenical and bismuth therapy, rather than alone.

Journal of Urology, Baltimore

58:397-484 (Dec.) 1947

*Wilms's Tumor in the Adult: Review of Literature and Report of 3 Additional Cases. G. L. Esersky, S. H. Saffer, C. E. Panoff and M. Jacobi.—p. 397.
Wilms's Tumor: Report of Three Year Cure. C. M. Burgess.—p. 412.
Hemangioma of Kidney: Report of 2 Cases. J. B. Lownes, S. Baron and H. Lipshutz.—p. 417.
Renal Varix. A. Sporer and R. Pollock.—p. 424.
Ureterovaginal Fistula: Repair of Ureteral Defect by Use of Bladder Flap. G. V. Caughlan.—p. 428.
Intraperitoneal Rupture of Urinary Bladder in Female: Report of Case. C. D. Tool.—p. 431.
Hysterectomy and Total Cystectomy with Bilateral Ureterocutaneous Implantation for Carcinoma of Bladder. Secondary Ureterosigmoidal Anastomosis for Complicating Ureterovaginal Fistula. D. A. Dreiling and A. Hyman.—p. 435.
Giant Bladder Calculus Associated with Upper Urinary Tract Lithiasis: Case Report. L. A. Maslow and J. Garnello.—p. 441.
Racial Incidence of Prostatism in Hawaii: Report of 172 Consecutive Cases. K. B. Conger.—p. 444.
Microscopic Diagnosis of Prostatic Tissue Obtained by Transurethral Resection: Analysis of 1,696 Cases. R. L. Satterlee.—p. 448.
Traumatic Rupture of Testicle. F. L. Senger, J. J. Bottone and W. F. Ittner.—p. 451.
Extensive Lymphangioma of Scrotum, Penis and Adjacent Areas: Report of Case. D. O. Ferris and C. L. Holmes.—p. 453.
Multiple Calcified Cysts of Scrotum: Case Report. H. V. Morley and J. W. Best.—p. 458.
Abdominal Wall Abscess Secondary to Perianal Abscess. H. J. Meisel, C. S. Gallion and J. M. Miller.—p. 461.
*New and Rapid Method for Control of Urinary Tuberculosis: Preliminary Report. G. E. Slotkin.—p. 464.

Wilms's Tumor.—According to Esersky and his associates increasing reports on Wilms's tumors in adults indicate that they are not as rare as has been presumed. Fifty-three cases have been reported previously, and to this number the authors add 3 cases of their own. The first patient, a man aged 47, died before the true nature of the disease had been recognized. Necropsy revealed an embryonal sarcoma (Wilms's tumor) of the right kidney with metastases to the liver, lungs and vertebrae, coronary thrombosis, bronchopneumonia and other disorders. The second case concerned a woman, aged 33, who was subjected to surgical treatment with the diagnosis of degenerating renal neoplasm. A nephrectomy was done on the left side. Examination of the surgical specimen established the diagnosis of malignant teratoma of the kidney (Wilms's tumor) with direct intrapelvic, extrarenal and intravascular invasion. The patient died two months after the operation. The third patient, a woman aged 24, was subjected to nephrectomy. An embryonal adenocarcinosarcoma of the kidney (Wilms's tumor) was found. The patient was given postoperative roentgen therapy and was still alive three years after the operation. The prognosis is unfavorable in this type of tumor. A patient with an unusually large renal mass and a high elevation in temperature, without evidence of urinary infection, should cause one to be suspicious of the possibility of Wilms's tumor

Control of Urinary Tuberculosis.—The study described by Slotkin was undertaken to determine whether there existed a more rapid and permanent control of inoperable or bilateral renal tuberculosis than the present therapeutic methods offered. With the advent of streptomycin such a control seemed to be available. Tubercle bacilli have a tendency to develop resistance against streptomycin. Mycobacterium tuberculosis has a protecting waxy cell wall. The same condition exists in Mycobacterium leprae. Long before the advent of antibiotics the author had conceived the idea that if a substance could be found to dissolve the protecting waxy wall, the process involved in inhibiting the growth might be enhanced. Knowing the existence of the same process in M. leprae, the oil of chaulmoogra and its derivative esters were experimented with in a few cases. After describing in vitro and animal studies on the effect of chaulmoogra oil on the sensitivity of Mycobacterium phlei to streptomycin, the author describes clinical observations on 6 active cases of inoperable and bilateral renal tuberculosis with secondary vesical symptoms. In the first 3 cases treatment was with the regular oil of chaulmoogra; later "moogrol," a more refined oil (a mixture of the ethyl esters of the fatty acids of the chaulmoogra series of oils) which is painless, more readily absorbable and nonirritating, was used. Each patient received 1 cc. of the oil intramuscularly daily for three days, then the dosage was increased to 2 cc. for four days. On the seventh day, the patient received 1 cc. of the oil and 1 Gm. of streptomycin. The treatment period lasted thirty days. The antibiotic is added to 16 cc. distilled water or sodium chloride solution and administered in eight doses of 2 cc. each, every three hours. All patients were hospitalized but ambulatory. The clinical results of this "softening and conditioning process" warrant further investigation, not only in the urologic tract but in all types of tuberculosis.

Michigan State Medical Society Journal, Lansing

46:1353-1478 (Dec.) 1947

Possible Infant Salvage at Florence Crittenton Hospital. S. W. Trythall.—p. 1385.
Rational Use of Diuretics in Congestive Heart Failure. E. H. Drake.—p. 1389.
Michigan Wants Excellent Nursing—Two Kinds. Grace Ross.—p. 1395.
*Parathyroid Extract and Diuresis. R. C. Moehlig and H. L. Abbott.—p. 1397.
Control of Blood Loss During Delivery. D. M. Shook.—p. 1402.
Treatment of Common Respiratory Infections. H. V. Dwyer.—p. 1407.

Parathyroid Extract and Diuresis.—Moehlig and Abbott direct attention to the diuretic effect of parathyroid extract, which has been known for some time. They present 2 case histories which illustrate the favorable effect of parathyroid extract. First, in a man aged 54 oliguria developed following treatment with sulfadiazine and sodium bicarbonate. The patient began to pass increasing quantities of urine on the second day of treatment with parathyroid extract. The patient was given 2 cc. (200 units) of this extract by intramuscular injection on four successive days. On the fifth and sixth days he was given 1 cc. and 0.5 cc., respectively. After that, the drug was discontinued because of the striking improvement. Second, a woman aged 36 was hospitalized with generalized urticaria, edema and sporadic convulsions, attributed to the ingestion orally of four tablets (25,000 units each) of penicillin. Treatment with diphenhydramine ("benadryl") caused exacerbation of the symptoms, particularly the edema. Diuresis finally began, and the edema subsided after the second injection of 2 cc. of parathyroid extract. The authors stress that the diuretic effect is directly proportional to the degree that calcium is mobilized in the blood.

Pennsylvania Medical Journal, Harrisburg

51:241-384 (Dec.) 1947

Future Status of General Practitioner. W. M. Johnson.—p. 265.
Penicillin Treatment of Sinus Infection. F. W. Davison.—p. 272.
Brucellosis. W. J. Fetter and G. E. Crum.—p. 276.
*Factors Influencing Immediate Survival Following Coronary Thrombosis with Myocardial Infarction. J. B. Tredway.—p. 280.
Infectious Diarrhea of Newborn: Report of an Epidemic. J. A. Ritter, Rose R. O'Connell and E. Lucente.—p 285.
Preventive Medicine in Hospital Practice. T. McC. Mahon.—p. 290.

Factors Influencing Survival in Coronary Thrombosis.—Tredway studied cases of acute myocardial infarction in order to ascertain what prognostic guides may give information as to the immediate outcome of the attack. The data were obtained only from cases of classic myocardial infarction, the diagnosis being based either on clinical criteria and unequivocal electrocardiographic evidence or on observations at necropsy. The series consists of 54 patients, of whom 21 died and 33 survived the acute attack. On the basis of his survey Tredway regards the following manifestations presented by a patient with acute myocardial infarction to be of bad prognostic import as far as survival in that attack is concerned: a past history of diabetes; previous infarction; congestive failure or vascular disease other than hypertension; epigastric pain; dyspnea; tachycardia; a pulse pressure of 20 mm. of mercury or less; evidences of shock; manifestations of congestive failure; irregularities of rhythm, particularly auricular fibrillation; either an elevated blood urea nitrogen level or blood sugar determination in the absence of renal disease or diabetes; a prolonged auriculoventricular conduction time.

Psychosomatic Medicine, Baltimore

9:353-408 (Nov.-Dec.) 1947

Role of Somatic Trigger Areas in Patterns of Hysteria. Janet Travell and N. H. Bigelow.—p. 353.
Rorschach Tension Score and Diurnal Lymphocyte Curve in Psychotic Subjects. L. Phillips and F. Elmadjian.—p. 364.
Psychosomatic Considerations in Peptic Ulcer. M. D. Zane.—p. 372.
*Relation of Group Morale to Incidence and Duration of Medical Incapacity in Industry. K. Brodman and L. P. Hellman.—p. 381.

Group Morale and Duration of Medical Incapacity in Industry.—The investigation of Brodman and Hellman was carried out on 600 employees of a mail order firm in New York. The relation between group influences and the duration of medical incapacity was investigated, using medical absenteeism as the measure of medical incapacity. No correlation was found between absence for long illnesses and lateness. However, in each quarter those departments in which employees were frequently absent for short illnesses were also those in which employees were frequently late. Since the frequent occurrence of lateness is a concomitant of poor morale, it appears that those departments in which employees are frequently absent for short illnesses are those in which the morale is poor. Medical incapacity is thus related to group morale. The data indicate that different work groups have dissimilar morale, that a person's work morale is decidedly influenced by the group in which he works and that group morale is intimately related to the occurrence and duration of short medical incapacities.

Puerto Rico J. Pub. Health & Trop. Med., San Juan

23:3-180 (Sept.) 1947

Studies on Genus Shigella. L. M. González, P. Morales Otero and J. Enrique Pérez.—p. 3.
*Nutritional Status of Puerto Rican Rural Community in Relation to Its Dietary Intake. Una Robinson and R. M. Suárez.—p. 100.

Nutritional Status in Rural Puerto Rico.—The report by Robinson and Suárez deals with a survey of the nutritional status and dietary intake of a population sample in a rural community of Puerto Rico. Its purpose was twofold: (1) to determine the dietary intake and its adequacy and (2) to study the correlation of said intake with the nutritional status. The dietary studies showed that the diets were conspicuously low in calcium, vitamin A and riboflavin and that all other dietary essentials failed to measure up to the recommendations of either the National Research Council or to a more conservative standard elaborated for Puerto Ricans. These diets were conspicuously low in milk and yellow and green vegetables. Physical examinations revealed many signs of nutritional deficiencies. Sixty-one per cent of the subjects were more than 5 per cent underweight; 73 per cent had dental caries or had lost some teeth; 79 per cent had slight or moderate signs of vitamin A deficiency; 95 per cent, of riboflavin deficiency; 28 per cent, of nicotinic acid deficiency, and 48 per cent, of ascorbic acid deficiency.

Virginia Medical Monthly, Richmond

74:543-595 (Dec.) 1947

Medical Progress During Past Century. R. H. Shryock.—p. 543.
Eighteen Hundred and Twenty: The Virginia Doctor and His Times. W. B. Blanton.—p. 547.
Acute Peripheral Arterial Embolism and Thrombosis. E. L. Lowenberg.—p. 551.
Treatment of Severe Compound Fractures of Foot. R. D. Butterworth.—p. 560.
Cooperation Between Oculists and General Practitioners. F. P. Smart.—p. 564.
Medical Public Relations. H. S. Johnson.—p. 567.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted. Single case reports and trials of new drugs are usually omitted.

Lancet, London

2:857-896 (Dec. 13) 1947

*Absorption of Penicillin Given by Mouth. H. C. Stewart and J. R. May.—p. 857.
Speech After Repair of Cleft Palate. F. H. Bentley and I. Watkins. —p. 862.
Trilene Analgesia: Simple Apparatus for Self-Administration. J. T. Hayward-Butt.—p. 865.
Holt's Diphtheria Toxoid (P.T.A.P.) Al PO_4 Content, Purity, Ageing, and Durability of Immunity. G. Bousfield.—p. 867.
Antistin In Treatment of Allergic Diseases. C. J. C. Britton.—p. 870.

Absorption of Penicillin Given by Mouth.—Stewart and May have tried to determine the relative importance of the factors governing the absorption of penicillin given by mouth, but made no attempt to treat actual infections; all the results were obtained in normal healthy adults. They found that in order to insure the best possible absorption, penicillin by mouth should be given on an empty stomach. The use of capsules gave results inferior to those obtained with the same dose in aqueous solution. The destructive effect of gastric acidity is only of importance when the p_H is less than 3. Most of the penicillin is absorbed in the upper part of the small intestine. Destruction of penicillin by penicillinase in the upper part of the digestive tract is negligible. Dextrose is a convenient source of energy which can be given with penicillin and often enhances the result. The most important factor influencing the absorption of penicillin seems to be the unexplained individual variations in the absorptive capacity of the intestine. The penicillin should be given in about 4 ounces (118 cc.) of a 5 to 10 per cent solution of dextrose, containing about 20 grains (1.29 Gm.) of sodium bicarbonate or citrate, before meals, and not less than three hours, preferably four hours, after the previous meal. The dose should be ten times as great as the dose of intramuscular penicillin that produces the blood penicillin levels required.

Medical Journal of Australia, Sydney

2:589-616 (Nov. 15) 1947

Anesthesia in Labor and Cesarean Section. C. N. Paton.—p. 589.
Local Anesthesia in Obstetrics. R. Mackey.—p. 593.

2:617-648 (Nov. 22) 1947

*Preliminary Report on Fish Poisoning at Fanning Island (Central Pacific). S. G. Ross.—p. 617.
Anticonvulsant Properties of Creatinine. J. F. Cade.—p. 621.
New Formation of Smooth Muscle in Lung. K. M. Bowden.—p. 623.

Fish Poisoning at Fanning Island.—Ross says that between February 1946 and April 1947 fish poisoning occurred in 95 persons in a population of 224 persons on Fanning Island in the central Pacific area. The symptoms of this poisoning are slow pulse, contracted pupils, numbness and sensation of tingling over the whole body, especially around the lips and at the fingertips. Gastrointestinal symptoms (epigastric pain, diarrhea and vomiting) are present in 75 per cent of cases. The symptoms are becoming more and more severe and nervous features more prominent. The recovery is extremely gradual, and weakness persists for several weeks. Cats, dogs and domestic ducks that are fed poisonous fish experimentally or accidentally develop ascending paralysis in eight to twelve hours, the paralysis lasting from three to five days. Ten different species of fish have already been classified as poisonous at Fanning. Prior to 1946 these fish were eaten without any ill effect. The areas in which the poisonous fish are caught correspond with places where the American army dumped war materials in July 1945. It is suspected that the plankton and algae as well as crustaceans and seaworms on which fish feed contain a poisonous principle emanating from deteriorating dumped war material. The effect of the poisonous agent at Fanning is similar to that of the poison isolated from sea plankton around San Francisco, where this agent was responsible for many cases of shellfish poisoning and was found to belong to the class of alkaloids.

Proceedings of Royal Society of Medicine, London

40:761-848 (Nov.) 1947. **Partial Index**

Transmeatal Attico-Antrotomy in Chronic Tympanomastoid Suppuration. A. Tumarkin.—p. 761.
Some Experiences with Bone Tumors. J. F. Brailsford.—p. 787.
Injuries to Bladder. R. A. Mogg.—p. 795.
Injuries of Urethra. D. S. Poole-Wilson.—p. 798.

Nordisk Medicin, Gothenburg

36:2079-2126 (Oct. 17) 1947. **Partial Index**

Hospitalstidende

Experiences in Intraspinal Administration of Penicillin in Treatment of Purulent Meningitis. O. Bentzen and H. Jørgensen.—p. 2085.

Norsk Magasin for Lægevidenskapen

*Primary Atypical Pneumonia. B. Knutsen.—p. 2099.
Peritoneal Irrigation in Anuria. B. Fretheim and O. Selvaag.—p. 2106

Primary Atypical Pneumonia.—Knutsen says that since Feb. 1, 1946, 86 certain cases and 24 probable cases of primary atypical pneumonia were seen at Drammen Hospital. In the course of a year the disease constituted over 37 per cent of the cases of pneumonia treated in the hospital. Most of the cases appeared as an epidemic in the fall of 1946. The disease was benign, with few complications but with protracted course. In the severest cases the cold agglutination titer continued high for weeks; in the mildest cases the titer fell rapidly. Penicillin or sulfonamide drugs were of no value except in a few cases with signs of bacterial complication. In 3 cases there was an erythema multiforme exsudativum, regarded as a complication of the primary atypical pneumonia, perhaps by activation of a virus. In 3 of the 4 samples of convalescent serum sent to him Eaton demonstrated neutralizing antibodies against the Eaton virus, indicating either present or past infection.

Presse Médicale, Paris

55:845-856 (Dec. 20) 1947. **Partial Index**

*Local Injections of Penicillin in Treatment of Adnexa. M. Roux and P. Monod-Broca.—p. 845.
*Role of Sewage Water as Disseminator of Virus of Poliomyelitis. C. Kling.—p. 848.

Penicillin in Treatment of Adnexa.—Roux and Monod-Broca treated 19 women who had salpingo-ovaritis with local injections of penicillin made at the level of the vaginal cul-de-sac. Eleven of the patients had an acute salpingitis characterized by a plastic reaction with bilateral painful soft swelling, mild rise of temperature and moderate leukocytosis. In 9 of these cases favorable results were obtained with five to six injections of 25,000 units of penicillin which were repeated every second day; complete recovery occurred in 6 patients, while the 3 remaining patients presented a small residual mass which subsided after three injections of "propidon" (Delbet's vaccine). Two patients with periuterine postpartum infection were therapeutic failures. Local treatment did not succeed in 2 additional patients with chronic salpingitis. Satisfactory results were obtained in 6 patients in whom an abscess that developed in the course of salpingitis was not amenable to any other treatment, general penicillin treatment included. In cases in which the sac of the abscess is accessible by the vaginal route, pus should be removed by puncture and penicillin should be injected into the cavity. Subperitoneal drainage may be employed in cases in which the sac shows an abdominal development, and penicillin should be introduced by means of a drain. If there is no suppurative sac or if it is not accessible, the injection should be made into the inflamed area around the adnexa. In periuterine infection local treatment with penicillin proved to be superior to general treatment with the agent and was effective when the latter failed. It is particularly indicated for periuterine lesions complicated by abscess.

Virus of Poliomyelitis in Sewage.—According to Kling, sewage water played an important part in the dissemination of the virus of poliomyelitis in two epidemics of poliomyelitis in two towns of Sweden during 1944. Sixty-three cases of poliomyelitis were observed in Katrineholm, a town of 11,570 inhabitants, i. e., a sick rate of 54.4 for ten thousand persons. Because of insufficient purification by filtration on sand, the sewage water contaminated the entire water system by which the drinking water was furnished to the population of this town. Fifty-three cases of poliomyelitis occurred in Halmstad, a town of 30,000 inhabitants, i. e., a sick rate of 17.6 for ten thousand. A sewage which apparently contained the specific agent caused contamination of the water which was furnished by one of the three systems of the town. Although experimental proof has not been obtained, the author believes that contaminated water which may be used by man for various purposes should be considered as one of the links which connects the sewage—into which the fecal ultravirus flows—with man who is susceptible to contamination.

Book Notices

Handbook of Diagnosis & Treatment of Venereal Diseases. By A. E. W. Metaxidian, M.D., Ch.B., D.P.H. Third edition. Cloth. Price, $5. Pp. 375, with 160 illustrations. Williams and Wilkins Co., Mount Royal and Guilford Aves., Baltimore 2. 1947.

This brings up to date the use of various therapeutic agents, especially penicillin, in the treatment of the various manifestations of syphilis and gonorrhea. Of the 362 pages in this book, the first 203 are devoted to syphilis in all its phases. Although some syphilologists might take issue with the author in the treatment of some phases of syphilis, especially the meager space he has given to fever therapy, on the whole the subject is well presented. The book is well illustrated with 160 pictures, twenty of these in color, and mostly photographs of the various manifestations of the diseases. The chapters are well organized, the subject matter well outlined and the book easy to read. Besides syphilis and gonorrhea other conditions commonly referred to the venereal disease department, such as lymphogranuloma inguinale, balanoposthitis, genital warts and paraphimosis, are briefly considered. As the title states, it is a handbook dealing with the diagnosis and treatment of veneral diseases and as such can be recommended to the busy practitioner and also the undergraduate medical student. To the general practitioner this book can be especially recommended.

The Cerebral Palsied Child and His Care in the Home. Prepared by Viola E. Cardwell, R.N., M.A. Staff Education for Nurses Engaged in Orthopedic Public Health Nursing. Cerebral Palsy Series: Revision of Pamphlet I. Paper. Price, $1. Pp. 196, with illustrations. Association for the Aid of Crippled Children, 580 Fifth Ave., New York 19, 1947

This dissertation deals with cerebral palsy in education, medical aspects, special therapies, general hygiene and social implications; it is well organized, rather complete in its coverage and well printed. Some aspects of the problem are underemphasized, as for instance the convulsive diatheses of the children. On the other hand some of the practical therapeutic procedures employed in physical therapy and in the teaching of self help and speech are well handled. The appendix giving standard forms employed in functional examinations and illustrating the various types of apparatus and the bibliography are of definite value. This book does not offer any new material or basic contributions to the field, since it consists primarily of quotations and excerpts from various sources. Much of the subject matter is controversial, and unfortunately this fact is not always indicated in the text. As an informational handbook for orientation of public health or orthopedic nurses, it is to be recommended. However, it does not fulfil the need for an authoritative book on the subject of cerebral palsy.

Importancia biológica del potasio. Por el Dr. Vicente Hector Cicardo, profesor titular de física biológica de la Facultad de ciencias médicas de la Universidad nacional de La Plata. Paper. Pp. 254, with 20 illustrations. Libreria y Editorial "El Ateneo," Florida 340, Córdoba 2099, Buenos Aires, 1947.

Professor Cicardo's monograph on the biologic importance of potassium is the most exhaustive written on this subject, as the 774 references discussed in the text testify. The book comprises sixteen chapters: 1, the origin and significance of potassium; 2, intracellular potassium; 3, potassium in the tissues; 4, extracellular potassium; 5, toxicity; 6, striated muscle and potassium; 7, cardiac muscle; 8, smooth muscle; 9, nerve; 10, central nervous system; 11, digestive secretions; 12, adrenals; 13, other glands of internal secretion; 14, shock; 15, anoxia, acid-base equilibrium, and 16, potassium in various pathologic conditions. On each of these subjects the author reviews the literature and presents the conclusions derived therefrom as well as from his own work.

Professor Cicardo's own work, presented in detail, was done mostly on frogs and includes cellular permeability to potassium and the influence of ions, specially of calcium; the influence of potassium on muscular contractions; the relation between acetyl choline and potassium, and the role of potassium in nerve transmission; the role of potassium in the mechanism of action of the adrenal glands. His experiments on the role of potassium in the production of shock were performed on dogs.

Although the role of potassium in the performance of all these biologic processes is undeniable, Professor Cicardo seems to have been carried away by his enthusiasm beyond the limits prescribed by the experimental facts. Professor Cicardo's theory of increased permeability of all cells in adrenal insufficiency is interesting and deserves attention.

Simplified Diabetic Manual with 163 International Recipes (American, Jewish, French, German, Italian, Armenian, etc.). By Abraham Rudy, M.D. Revised by Martin M. Nothman, M.D., Instructor in Medicine, Tufts College Medical School, Boston. Introduction by Dr. Frederick M. Allen. Fourth edition. Cloth. Price, $3. Pp. 216, with illustrations. W. Barrows & Co., Inc., 114 E. 32nd St., New York 16, 1947.

With the exception of the chapters devoted to the various menus, especially those concerned with the foods of the various nationalities, this book is too cursory to be helpful to the diabetic person or to the physician concerned with the disease. In the section devoted to "marriage in diabetes," for instance, charts indicate that diabetes is hereditary and yet the closing sentence states that "congenital diabetes is extremely rare." This is confusing to the layman. The chapter on insulin fails to make clear to the average reader the distinctions concerning the three now well known types, for he fails to be specific and sufficiently descriptive in his discussion concerning the time of administration and the actual length of the effect of the various insulins. For example, when writing on globin insulin he states "that one injection may be enough." When is it not enough? How can the reader judge? It is confusing too that the chapter on "diabetes in children" precedes those on "marriage in diabetes" and "diabetes and pregnancy," which two are followed by treatment of the elderly diabetic. The material could well be better arranged. This book is invaluable to one interested in menus but not especially helpful to those concerned with the progress made in treatment of diabetes.

Physical Medicine in General Practice. By William Bierman, M.D., Attending Physical Therapist, Mount Sinai Hospital, New York. With a Chapter on Medical Rehabilitation by Dr. Sidney Licht. Second edition. Cloth. Price, $8. Pp. 686, with 310 illustrations. Paul B. Hoeber, Inc., 49 E. Thirty-Third St., New York 16, 1947.

This carefully planned book not only covers the complete field of physical medicine but also has added interest by numerous clear illustrations for visual teaching. The theme is developed from simple subjects to those requiring more advanced knowledge of basic sciences. The chapters on climatotherapy and spa therapy gives a practical insight into the indications for these physical mediums. The chapters on heat, light and electricity reflect the broad experience of the author in research and use of these measures. The important details of massage, exercise and occupational therapy are included. Dr. Sidney Licht's excellent chapter on rehabilitation shows his realization of the importance of considering the patient as a total personality. Psychologic and physical factors are presented in their proper perspective. The paragraphs on paraplegia and amputations as well as those related to speech, vision and hearing are authoritative from the background of his experience as a medical officer in the recent war and as present consultant in the Veterans Administration. The transition through formal treatment to diversional and work therapy is well developed. In the last third of the book Dr. Bierman includes plans for departments of physical medicine and for treatment. Emphasis is given to professional responsibility, medicolegal problems, dangers and cautions. Diseases of the various systems are discussed in light of indications or contraindications for physical treatment. At the end of each chapter is a list of references for the benefit of readers who wish to pursue certain subjects in greater detail.

One wonders about the title of the book after reading it. Will the general practitioner be able to use this book for easy reference? There is no question but that it will be a useful volume for the physiatrist, physical therapist and occupational therapist. Other physicians with interest and groundwork in physical medicine will, no doubt, appreciate its subject matter. Perhaps, in justice to the author, one should quote from the preface: "I have attempted to emphasize those sections of physical medicine which the general practitioner may be reasonably expected to apply in his practice. I have also made reference to important therapeutic considerations which are beyond the scope of the general practitioner in order that he may become aware of them even though he cannot utilize them himself."

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

ALCOHOLISM AND HEREDITY

To the Editor:—**Are there statistics to prove that the children of alcoholic persons are more apt to be imbeciles?**

M.D., Monterrey, N.L., Mexico.

ANSWER.—Belief that alcoholism in man affects the germ plasm lacks substantiation. Since 35 to 40 per cent of alcoholic addicts come from families with epileptic, psychotic or feebleminded members, it is not surprising that the alcoholic persons themselves show a high incidence of these disorders, some of which are known to be hereditary. Excessive drinking cannot be expected to prevent their transmission. Boss (*Monatschr. f. Psychiat. u. Neurol.* **72**:204, 1929) showed that these defects do not appear more frequently in the children of unstigmatized alcoholic persons than they do in the general population.

Roe (*Quart. J. Stud. on Alcohol* **5**:378-393, 1944) reports convincing evidence against hereditary factors caused by alcoholism of parents. She compared adult adjustments of children of alcoholic parents to a control group of children of normal parents, both groups having been raised in foster homes. Significant differences were not found. Greater consumption of alcohol did not occur in the offspring of alcoholic parents than in the control group.

EPIPHYSIAL ARREST

To the Editor:—**A boy now aged 12½ years was stricken by poliomyelitis at 2 years of age. His left leg was badly damaged and suffered the loss of the iliopsoas muscle, quadriceps muscle, the peroneus group and others. There is pronounced atrophy and shortening of the left leg of about 1¾ inches (4.5 cm.). The patient walks with a long leg brace (using the gluteus muscles). He is able to walk without a brace but is then more unsteady because of difficulty in locking the knee joint.**

The main problem at present and for the future appears to be the difference in length of the lower extremities. This boy comes from a family of medium height, and probably he will not be exceptionally tall. His present height is 4 feet 11 inches (149.86 cm.). Now is probably the time to consider an epiphysial arrest on the unaffected leg. Although there are many reports available recommending this procedure I am led to believe that the reported incidence of deformities following this operation is quite high and discouraging.

Regan and Chatterton (*J. Bone & Joint Surg.* 28: 265 [April] 1946), although recommending the operation, report deformities in 4 of 36 persons with epiphysial arrest. Therefore supracondylar shortening of the femur on the good side done at the end of the growth period, although a more formidable operation, seems more logical and safe to me.

Please give an opinion and estimate the damage that can be done to the spine, which has to make up by compensatory lordosis for the unilateral shortening, if one waits with an equalization by supracondylar shortening until the end of the growth period or young adulthood has been reached?

M.D., Wisconsin.

ANSWER.—The choice of operative procedure in a case such as that described should be made on the basis of the surgical training and experience of the surgeon who is doing the work.

Opinions with regard to equalization of leg length by epiphysial growth arrest on the normal leg, by femoral shortening after skeletal growth maturity has taken place or by lengthening of the short leg have been fairly well divided among the orthopedic surgeons who have had experience in dealing with this problem.

The most formidable of the three procedures is actual lengthening of the shorter extremity; this should not be undertaken in any instance in which the bones that are to be lengthened are decidedly atrophic from paralytic disuse.

If the spine is completely flexible and without evidence of structural scoliosis, no great damage may result from delaying surgical procedures until skeletal maturity has been achieved.

A more accurate equalization of leg length can be obtained through the resection of a carefully measured segment of the femur. The healing of the femur following such resection may be prolonged over a period of six months or more, and this procedure certainly does represent a much more formidable operative and postoperative program than is required by epiphysial growth arrest.

For the patient described, an arrest of growth of the distal end of the femur would be a much more simple and safe operation. In all probability, an arrest at this age would bring about approximate equalization of the length of the leg, by the time this boy is fully grown.

Deformities resulting from growth arrest operations have not been significant. In an occasional patient the arrest becomes complete for one femoral condyle before it does for the other, resulting in some degree of knockknee or bowleg. If the operation is thorough, with a bone graft laid across the epiphysial line, as described by Phemister, a complete checking of longitudinal growth from the lower femoral epiphysis can be anticipated within a period of three to five months and no deformity will result. In an infrequent instance as a result of the growth arrest the leg that was originally short may be a little longer than the other leg when full skeletal maturity has been reached. In no instance that has been recorded has this difference been significant.

SCALENUS ANTICUS SYNDROME

To the Editor:—**Give details on diagnosis of "scalenus anticus syndrome."**

What per cent of disability is ordinarily allowed for a simple fracture of the clavicle?

What is the latest and most acceptable book giving interpretation and per cent of disabilities allowed for various types of injury?

M.D., New Jersey.

ANSWER.—Symptoms of the scalenus anticus syndrome are as follows: The patient usually complains of pain over the outer surface of the shoulder on the involved side. This pain may extend down the arm or radiate up the back of the neck with referral to the seventh cervical spinous process (vertebral prominens). At times the pain may be referred along the course of the ulnar or median nerves in the arm and forearm. The pain can be relieved if the patients turns his head to the affected side or raises his elbow. Frequently there is tenderness of the scalenus muscle at its attachment to the first rib. Decreased sensation to all forms of stimuli occur in the arm and forearm; atrophy and total loss of sensation are seldom seen. Treatment is either palliative or surgical. The former is used in mild cases as exercise of the involved shoulder region in order to strengthen the trapezius and other muscles which elevate the shoulder girdle. In most cases surgical treatment is required. This consists of sectioning the scalenus anticus muscle and also any fibers of the scalenus medius which seem to be tense. In some cases resection of a cervical rib may be necessary. This syndrome was originally described by Naffziger of San Francisco. For an excellent description refer to the original article (Naffziger, H. C.: The Scalenus Syndrome, *Surgery, Gynec. & Obst.* **64**:119, 1937).

Usually in a simple fracture of the clavicle without displacement or overriding of the fragments there is no percentage of permanent disability because there is no disability.

Since the Industrial Commissions in the various states of the union operate individually, there is no publication on percentages of total, temporary or permanent disability that can be purchased. Write to the Industrial Commission in your state. They can give you the information you need.

TUBERCULOSIS IN DIABETIC PERSONS

To the Editor:—**What is the incidence of tuberculosis among diabetic persons as compared to that of tuberculosis in the general population. Can this information be broken down to reveal the percentage of cases observed in diabetic clinics versus those first seen in hospital wards (i. e., uncontrolled and complicated cases of diabetes mellitus) and those first observed in tuberculosis hospitals? Recent discussion in a diabetic clinic brought out the point that not a single case of tuberculosis had been seen during the time that chest surveying had been instituted at the clinic. My feeling is that controlled diabetes would not exhibit an increased incidence of tuberculosis, whereas it might be noted among persons with uncontrolled diabetes (hospitalized patients) or those already in tuberculosis hospitals.**

Jean P. Papps, M.D., Forest Hills, N. Y.

ANSWER.—Prior to the advent of insulin necropsies revealed that one fourth to one third of persons dead from diabetes also had tuberculosis. However, since 1926 tuberculosis in an active stage has seldom been found at necropsy in more than 6 or 7 per cent of diabetic persons. H. F. Root in 1934 (*New England J. Med.* **210**:1, 78, 127 and 192, 1934) published extensive observations on the association of diabetes and tuberculosis. He found that active tuberculosis occurred in diabetic patients at necropsy between two and three times as frequently as among nondiabetic patients. Among 750 children in whom there developed diabetes before the age of 15 years the reinfection type of pulmonary tuberculosis was more than thirteen times as frequent as in Massachusetts school children. Among adolescent diabetic patients who contracted the disease between the ages of 15 and 20 years, pulmonary tuberculosis occurred sixteen times as frequently as in Massachusetts high school students. There was roentgenologic evidence which suggested active pulmonary tuberculosis in 2.8 per cent of 1,373 adults with diabetes.

A. L. Banyai and A. V. Cadden (The Rationale of the Therapeutic Administration of Massive Doses of Vitamin A in Tuberculous diabetics, *Dis. Chest* **10**:133, 1944) reported that 2.6 per cent of a large number of diabetic patients were found to have pulmonary tuberculosis. Wiener and Kavee (*Am. Rev. Tuberc.* **34**:179, 1936) reported that 23.9 per cent of 909 diabetic patients had tuberculosis. However, this high figure is probably due to the large proportion of the patients in Montefiore Hospital, New York, who have tuberculosis. Himsworth (Pulmonary Tuberculosis Complicating Diabetes Mellitus, *Quart. J. Med.* **7**:373, 1938) has collected data which show that since the introduction of insulin pulmonary tuberculosis develops in 2.7 per cent of those with diabetes.

There is good evidence that the increased incidence of tuberculosis in diabetic patients now is for the most part among those whose diabetes has been uncontrolled or inadequately treated. When the two diseases are associated the diabetes is discovered before the tuberculosis in 65 to 80 per cent of the patients. Tuberculosis appears more frequently among those with severe forms of diabetes than among those with mild forms. For example, among those who had diabetic coma, in 8 per cent tuberculosis developed within three years, which is fourteen times the incidence of pulmonary tuberculosis in the general population. J. Kavee (Pulmonary Tuberculosis and Diabetes Mellitus, *Bull. Am. Acad. Tuberc. Physicians* **4**:147, 1940) observed pulmonary tuberculosis both in mild and in severe cases of diabetes at the Montefiore Hospital. However, the proportion of patients with pulmonary tuberculosis who had the severe form of diabetes was much greater than usual among diabetic persons of similar age. It has been generally observed that diabetic patients with pulmonary tuberculosis nearly always require insulin. Likewise, pulmonary tuberculosis in the presence of diabetes usually requires collapse therapy.

Kavee reported that among 332 patients who entered Montefiore Hospital only 17 had well controlled tuberculous lesions. In 15 of these cases the tuberculous lesions had not progressed or reactivated over a considerable period of observation, some as long as ten years. Since old inactive pulmonary tuberculosis seldom becomes reactivated and since minimal pulmonary lesions without symptoms, cavitation or positive sputum often recede in persons with well controlled diabetes, there apparently is little likelihood that persons with well controlled diabetes who are free from tuberculosis are any more likely to have primary lesions and the subsequent reinfection type of disease develop than are persons in the general population. Therefore, your contention apparently is correct.

Nevertheless, every diabetic patient whose condition is not adequately controlled should be kept under close observation, as such persons are two or three times more likely than others to acquire clinical tuberculosis. Both reactors and nonreactors to tuberculin should be closely guarded against contact with contagious tuberculosis, as first infection and reinfection are dangerous to them.

There is no reason to suspect that persons with well controlled diabetes are less likely to contract tuberculosis than those in the general population. Therefore, even the best controlled patients should be carefully protected against first infection and reinfection types of tuberculosis. Should clinical disease appear and show evidence of continued activity, collapse therapy should be promptly instituted.

RADIOIODINE

To the Editor:—**What are new trends or methods of treating cancer? A woman, aged 68, has a malignancy of the throat. She had had a complete series of high voltage roentgen therapy and had shown little or no improvement. The family have been reading about radioactive therapy and also the use of atomic therapy and would like to know the advisability of using that on the woman. I know nothing about such treatment and would like advice about the matter.**

M.D., Illinois.

ANSWER.—What is meant by "malignancy of the throat?" Without better information part of the question is unanswerable. The term "atomic therapy" is not familiar. "Radioactive therapy" probably means use of one of the radioactive isotopes. If by "malignancy of the throat" the correspondent by chance might mean cancer of the thyroid the answer would be that radioactive iodine has a limited value in certain types of the disease, its value being dependent on the results of preliminary tracer studies for iodine pick-up by the tumor. Nothing is known of any isotope of potential value in any other type of cancer which is primary in the area described and which is proved to be radioresistant to the roentgen ray. Even if the tumor is a lymphosarcoma, if it is resistant to roentgen therapy there would be no reason to hope that it would respond to a radioactive isotope.

ACROMEGALY

To the Editor:—**A man aged 30 presents some of the clinical features of acromegaly (increase in the length of bones of the hands) and hypogonadism (impotence, small penis and testicles, obesity of female type, scanty beard growth).**

Roentgen examination of the skull revealed an enlargement of the pituitary fossa (25 mm. by 11 mm.) with destruction of the dorsum sellae and the anterior clinoid processes. His basal metabolic rate was minus 15 per cent; the cholesterol content of the blood was 400 mg. per hundred cubic centimeters. He has no glycosuria. The blood sugar curve was rather flat. Eye examination did not reveal abnormality of the fields of vision or evidence of choking of disks.

The patient's only complaint is impotence. He claims to have had normal sexual functions some eight to nine years ago. There occurred a sudden increase in weight four years ago during a particularly strenuous period (during the Italian Campaign).

What substitutive treatment is indicated? Is irradiation of the pituitary imperative or could it wait until signs of further extension of the tumor develop?

Would chorionic gonadotropin be useful, and to what extent could it cure the patient's impotence? What is the prognosis?

M.D., Newfoundland.

ANSWER.—In acromegaly there is a disturbance of many of the glands of internal secretion, and of course the pituitary gland is one which has to do with sexual desire and ability. I believe that administration of the hormones is indicated. The substance used may be "Antuitrin S" (chorionic gonadotropin) or alcohol extracts of anterior pituitary, testicles and the adrenals, with which there has been some success and which may be administered every other day until a series of twelve injections has been given.

Irradiation of the pituitary is not absolutely essential unless signs of further extension of the tumor develop.

The prognosis in such a case is poor, and the course of injections may have to be repeated on numerous occasions.

DERMATITIS PATCH TESTING

To the Editor:—**A patient, aged 60, a railroad agent, has a severe dermatitis on his legs, hands, arms and face. It has occurred at intervals during the last two years. I believe it is due to a rubber raincoat, similar to the type used by the Army. What specific substance in the raincoat would be likely to be responsible for the dermatitis? Might it be due to tetramethyl thiuram disulfide?**

Delmer E. Johnson, M.D., Alamosa, Colo.

ANSWER.—To incriminate the raincoat a patch test with the inside or the lining of the raincoat should be positive. Even this would not be absolute proof, because it is most unusual for a contact dermatitis to develop on parts which are not in contact with the article of wearing apparel. Raincoats are not usually worn in contact with the skin, and it is hardly conceivable that a chemical in the raincoat or on its external surface would leach out in sufficient quantity to penetrate through the clothing and reach the skin.

Once the raincoat has been established as the cause of the dermatitis, the manufacturers of it should be requested to give the composition of the material from which it was made and the chemicals which it contains.

The Army had raincoats made of vinyl resin films ("vinylite," "koroseal"), of fabrics coated with these films and of rubberized fabrics.

It has been found that plasticizers and stabilizers are the most common sensitizers in the vinyl resin films. In rubber materials the usual sensitizers are the accelerators, the antioxidants and the chemicals formed on the surface of the rubber by the so-called acid or vapor cure, in which sulphur monochloride is the curing agent. Tetramethyl thiuram disulfide ("tuads") is only one of the many rubber accelerators which has been reported as causing sensitization dermatitis.

When the chemicals in the raincoat have been ascertained, patch tests of the patient with each of them, using the proper technic, may reveal the chemical to which the patient is sensitive.

References:

Schwartz, L.; Tulipan, L., and Peck, S. M.: Occupational Diseases of the Skin, ed. 2, Philadelphia, Lea & Febiger, 1947.

Schwartz, L., and Peck, S. M.: Dermatitis from Wearing Apparel. J. A. M. A. **128**: 1209-1217 (Aug. 25) 1945.

HOOKWORM INFESTATION

To the Editor:—**Are there reported cases of bronchial asthma caused by hookworm infestation? What is the treatment other than elimination of the parasite from the alimentary canal?**

Herbert A. McClure, M.D., Lake City, Fla.

ANSWER.—Infestation with parasitic worms produces a hypersensitivity that is evidenced on skin test by an immediate wheal from intradermal injection of an extract and the finding of transferable antibodies (reagins). These facts provide the basis for the possibility that allergic manifestations such as asthma can be produced by hookworm infestation. Reports of authenticated cases were not found in the literature. Elimination of the hookworm infestation is the logical procedure in such a suspected case.